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Organic Farming Can Have Much Greater Implications for Climate Change

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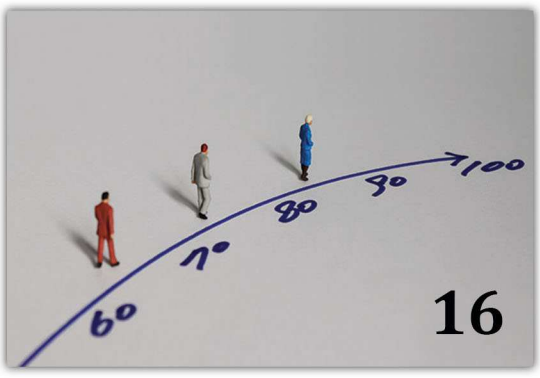

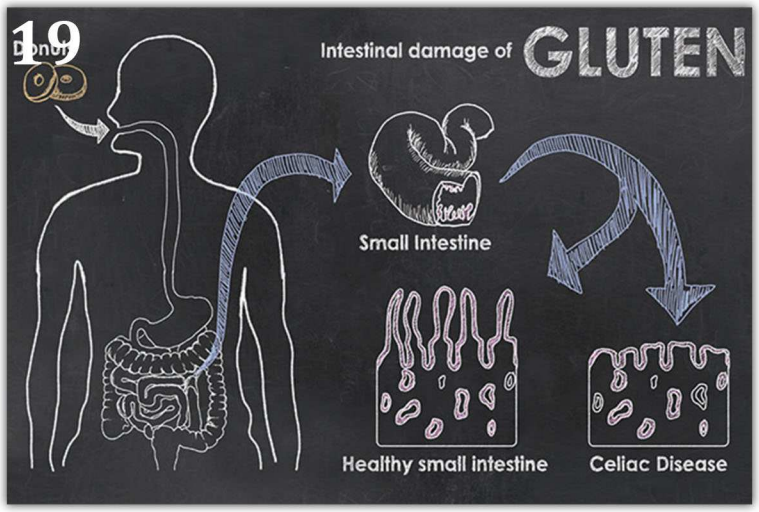

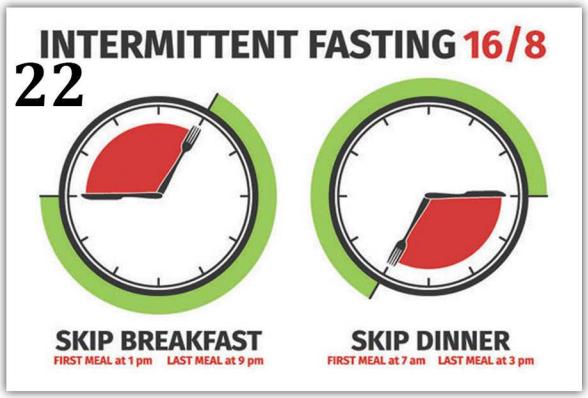

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A new study has used robotic screening for short-listing chemical compounds which could be 'prevent' malaria

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We are thrilled to bring to you nine articles on recent scientific advances which have the potential to affect lives including a treatment for gluten intolerance, a novel wireless brain pacemaker, effectiveness of probiotics on stomach flu, next generation drugs for malaria and many more.

Hope you find them intellectually stimulating!

Umesh Prasad

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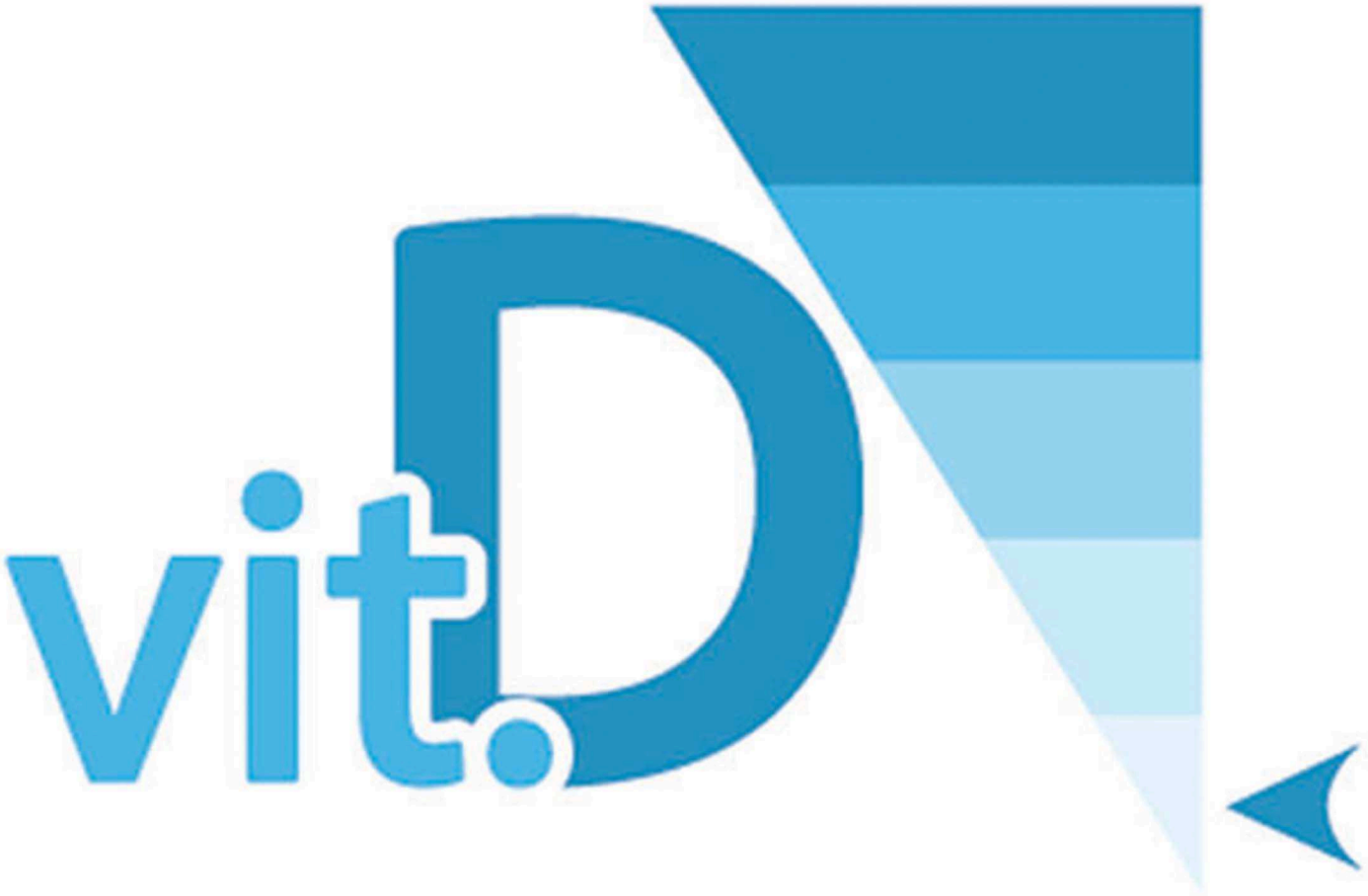
Magnesium Mineral Regulates Vitamin D *Levels in Our Body*

A new clinical trial shows how mineral magnesium has the ability to regulate vitamin D levels in our body

Magnesium, an essential micromineral is needed in large amounts for our body as it has multitude of health benefits. Magnesium is known to maintain functions of nerves, muscles, in regulating heartbeat, regulating blood sugar and maintaining strong and healthy bones. Magnesium is also known to improve sleep quality and prevent headaches including migraines. Green leafy vegetables and some fruits like banana and raspberries are suitable food sources of magnesium as they are enriched with this mineral. Magnesium is also found in nuts, legumes, sea food and black chocolate. The recommended daily dose for magnesium varies from 300-400 mg depending upon gender. When protein-rich food is consumed or there is intake of calcium and vitamin D levels, they are seen to increase body's demand for magnesium. Magnesium is largely ignored as a supplement and is hardly recommended by doctors.

Vitamin D is a fat-soluble vitamin responsible for maintaining normal levels of calcium and phosphorus in our blood as it helps to absorb calcium and thus supports to form and maintain strong bones. Vitamin D may provide protection and also decrease an individual's risk of developing diseases like osteoporosis, hypertension and cancer. Vitamin D levels in our body are important for colorectal cancers as has been highlighted in observational studies. Deficiency of vitamin D is a big public health problem affecting millions worldwide of all age groups, in fact over a billion people across the globe are thought to be deficient in vitamin D and this problem is prevalent in both



developed and industrialized nations. Though vitamin D deficiency can be overcome by spending 15-20 minutes daily under the sun with one's 40 percent of skin surface exposed, this runs high risk of developing skin cancer. Vitamin D fortification via supplements is now routine in the public health care system.

Association between magnesium and vitamin D

Previous studies have shown that magnesium affects enzymes (metabolic pathways) which are required to activate vitamin D thereby indicating the need of magnesium for vitamin D to be effective. And low amounts or a deficiency of magnesium means low vitamin D as well because production of the vitamin gets inhibited. A follow-up to the previous observational studies linking the role of magnesium and vitamin D in preventing colorectal cancer, researchers in the current study set out to understand the exact association between magnesium and vitamin D levels to understand what influence it could have on colorectal cancer and other diseases. A randomized controlled trial was conducted in which around 180 participants who were part of Personalized Prevention of Colorectal Cancer Trial (PPCCT) and were at risk of developing colorectal cancers were included. A random grouping into two groups was done; the first group was given doses of magnesium supplements according to their daily intake of magnesium as part of the diet. The second group was given a placebo which was 'identical' to magnesium capsules. While this treatment was being conducted, levels of vitamin D metabolites in participant's blood were measured.

Results showed that magnesium supplements which the participants took, 'interacted' with the vitamin D circulating in their blood and this increased the levels of vitamin D if levels were too low. If vitamin D encountered was too high, then magnesium supplements reduced it. Magnesium was seen to be 'regulating' vitamin D levels and optimizing them. This control by magnesium prevents both vitamin D deficiency and toxicity and is attributed to the effect magnesium has on the enzymes involved in production of vitamin D in our body.

This study published in *American Journal of Clinical Nutrition*, is the first evidence which shows that magnesium plays a key role in optimizing vitamin D levels in our body and can guide prevention of disease conditions directly or indirectly linked to vitamin D concentration. These findings could also explain why some could also explain why some times taking vitamin D supplements has no effect on its levels in the body because without adequate magnesium, vitamin D may not be useful as it won't get metabolized. The study suggests that if daily diet intake of magnesium is not sufficient in a person, then magnesium supplements should be advised. Magnesium is a mineral which is under-consumed and its supplements are also rarely prescribed but this study advises that the scenario needs to change. Our daily diet must include green leafy vegetables, beans, whole grains and fatty fish to get our daily requirements of magnesium as more than half the populations even in developed countries is consuming a magnesium deficient diet.

Source

Qi Dai et al., 2018, 'Magnesium status and supplementation influence vitamin D status and metabolism: results from a randomized trial', *The American Journal of Clinical Nutrition*, Vol. 108, no. 6, DOI: http://dx.doi.org/10.1093/ajcn/nqy274 ■

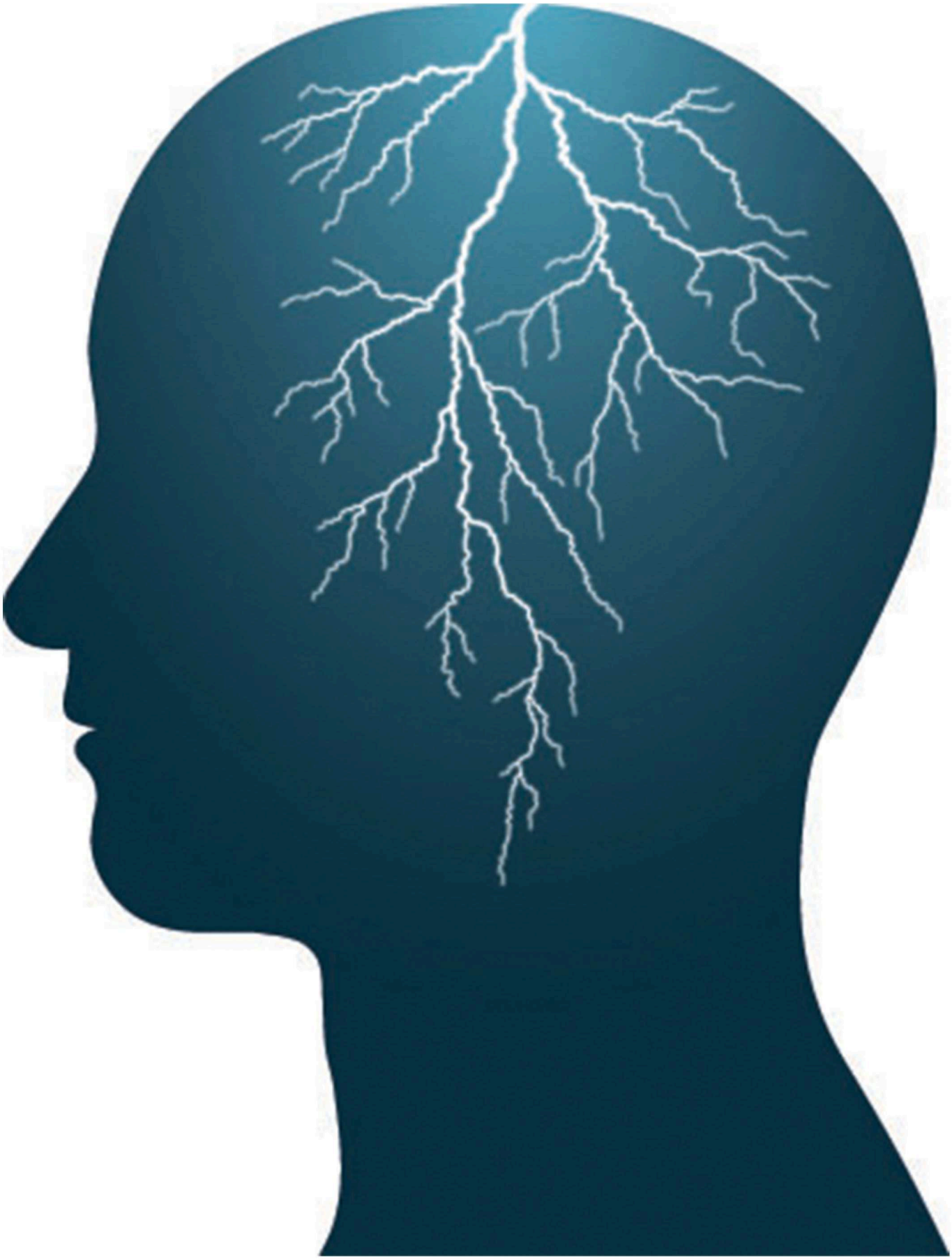
A Wireless "Brain Pacemaker" That Can Detect *and Prevent Seizures*

Engineers have designed a wireless 'brain pacemaker' which can detect and prevent tremors or seizures in patients suffering from neurological disorders

According to World Health Organization (WHO) neurological disorders affect more than one billion people worldwide and it causes more than 6 million deaths annually. These disorders include epilepsy, Alzheimer's disease, brain stroke or injuries and Parkinson's disease. The impact of these diseases is present in both developed and developing countries and many times treatment is unavailable due to lack of a proper health system, trained personnel or other factors. The global population is ageing and according to WHO, in the next 30-40 years more than half the population will be over 65 years of age. It is imperative to understand that neurological disorders are going to be a huge health burden in the near future.

A 'pacemaker' for the brain

Engineers from University of California Berkeley USA have designed a novel neurostimulator which can simultaneously listen ('record') and also stimulate ('deliver') electric current inside the brain. Such a device can provide a perfected personalized treatment for patients suffering from neurological disorders particularly Parkinson's disease and epilepsy. The device is coined WAND (wireless artifact-free neuromodulation device), and it could be also called as a 'brain pacemaker' similar to the heart pacemaker - a tiny, battery-operated device which is able to sense when the heart is beating



irregularly and then delivers a signal to the heart to achieve the desired correct pace. Similarly, the brain pacemaker is able to wirelessly and autonomously monitor the brain's electrical activity and once it has learned to identify signs or features of a tremor or seizure in the brain, the device can self-adjust stimulation parameters by delivering the 'correct' electrical stimulation when something is not in order. It is a closed loop system which can record as well as stimulate alongside and is able to adjust the different parameters inreal-time. WAND is able to record electrical activity in the brain over more than 125 channels in a closed-loop system. For a practical demonstration, researchers showed that WAND was able to recognize and take appropriate measures to successfully delay extremely specific arm movements in primate monkeys (rhesus macaques).

Key points

- Engineers have designed a novel neurostimulator which can simultaneously listen ('record') and also stimulate ('deliver') electric current inside the brain.
- The device can provide a personalized treatment for patients suffering from neurological disorders particularly Parkinson's disease and epilepsy.

Challenges with previous devices

One of the major challenges in finding the right therapy for a patient having a neurological condition is the lengthy duration of first finding a procedure and then the high costs involved. Any such device could very effectively prevent tremors or seizers in patients. However, the electrical signatures which come before the actual seizure or a tremor are extremely subtle. Also, the frequency and strength of the desired electrical stimulation which has the ability to prevent these tremors or seizures is also very sensitive. That is the reason why small adjustments for particular patients usually takes years before any such device is able to provide an optimal treatment. If these challenges are adequately met, there can be a definite increase in outcomes and accessibility.

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In a new study published in *Nature Biomedical Engineering,* researchers wanted the device to give the best possible outcome for a patient by providing an optimal stimulation. This is achievable only by listening as well as recording the patterns or neural signatures. But, recording and stimulating electrical signals is very challenging as large pulsations which are delivered by stimulation can overwhelm the electrical signals in the brain. The issue with current deep brain stimulators is that they are unable to 'record' and at the same time 'deliver' stimulation to the same region of the brain. This aspect is the most crucial for any closed-loop therapy and no such device is currently available commercial or otherwise.

This is where the exceptionality of WAND comes into the picture. Researchers designed WAND

customized circuits which can 'record' complete signals from both the subtle brain waves as well as from stronger electrical pulsations. The subtraction of signal from electrical pulsations results in a clearer signal from the brain waves which none of the existing devices are able to do. Thus, simultaneous stimulation and recording in the same region of the brain conveys us the exact happenings which can be used to design an ideal therapy. WAND allows reprogramming for use in different applications. In a live experiment on monkeys, WAND device was proficient in detecting neural signatures and was then able to deliver the desired electrical stimulation. For the first time, a closed-loop system has been demonstrated to perform these two tasks together.

Source

Andy Zhou et al 2018, 'A wireless and artefact-free 128-channel neuromodulation device for closed-loop stimulation and recording in non-human primates', *Nature Biomedical Engineering*,
DOI: https://-doi.org/10.1038/s41551-018-0323-x ■

Probiotics Not Effective Enough in Treating 'Stomach Flu' in children

Twin studies show that expensive and popular probiotics may not be effective in treating 'stomach flu' in young children.

Gastroenteritis or commonly called as 'stomach flu' affects millions of young children worldwide. It is caused by bacteria, viruses or parasites and though it is not a life-threatening disease but it's a huge burden on medical care as it is a common cause of hospitalization. There is no quick treatment for pediatric acute gastroenteritis apart from giving children fluids mainly to prevent dehydration, and some medicine for nausea and ample rest. Since there is lack of any proper treatment, doctors are prescribing probiotics in treating children who have acute gastroenteritis.

Deeper understanding of the microbiome – millions of friendly bacteria, viruses, fungi etc. which are believed to benefit the human body has fueled the growth of probiotics. Probiotics is primarily safe live microorganisms also called 'friendly' or 'good' bacteria which are thought to fight stomach infections. They are believed to restore normal balance of bacteria in our digestive system and they also boost our immunity by improving our immune system. Many smaller studies have shown that probiotics may be useful but such results have been limiting.

Probiotics not effective after all?

A new vigorous study[1] published in *New England Journal of Medicine*, involving 1,000

children (3 months to 4 years of age) gives first evidence that probiotics may not be the best or useful approach especially for young children. The authors aimed to generate conclusive evidence either for or against use of probiotics in infants and toddlers suffering from acute gastroenteritis. Researchers evaluated a most commonly prescribed probiotics called Lactobacillus rhamnosus GG (LGG) which has a version ideally suited for babies and young children. The study involved 971 children who were given treatment over 3 years from 2014 till 2017 at emergency centers at geographically diverse medical centers across the United States. The children were chosen if they displayed symptoms of gastroenteritis like loose stool, vomiting, diarrhea or intestinal infection. A precondition was that they had not consumed any probiotics for at least 2 previous weeks.

Half of the children were randomly chosen to receive probiotic LGG twice daily for five days, others consumed an identical looking placebo. Apart from this, children were given standard clinical care. Researchers or the parents didn't know at this point which of the children were given probiotics. It was seen that all children showed same symptoms and identical recovery – whether they were given probiotics or placebo – for instance every child had diarrhea for two days. A comparison between infants and toddlers was also made. Patients who had taken probiotics were tested to see whether gastroenteritis was caused by virus or bacteria. The probiotic was also independently tested for purity and strength. Researchers came to only one conclusion –probiotic LGG made no difference. The probiotic didn't help either in curbing vomiting or diarrhea.

In a second study[2] conducted in Canada also published in *New England Journal of Medicine,* 886 children (aged 3 months to 2 years) who had gastroenteritis received a five-day course of probiotic containing Lactobacillus rhamnosus R001 and Lactobacillus helveticus R0052 or a placebo (commonly given in South Asia). In this study also no difference was seen between the two groups of children given probiotics or placebo.

These twin studies in Canada and in the United States conclude that two popular probiotic formulations which were tested had simply no effect on the children and therefor it can be concluded that probiotics should not be used for gastroenteritis either by doctors or by parents on their own. Doctors must consider totality of these evidences and should incorporate the same in intervention strategies for acute pediatric diarrhea. However, authors make it clear that their studies are about the effect two popular probiotics on gastroenteritis in young children and it does not claim that probiotics have to be completely eliminated for everything. Though safe, probiotics are still expensive and unnecessary 'pills containing bacteria' and it is better for the children to consume good food like yogurt, fruits or vegetables instead.

Such studies are also crucial in making advances towards eliminating medications which have zero effect. Probiotics are being sold for being effective in all kinds of ailments – from digestive health to obesity and heart and also for mental health. This is a multi-million-dollar industry; however, experts urge that there is need for stricter regulations around probiotics as they come under dietary supplements which otherwise do not require approval unlike other over-the-counter drugs. And most of the research on goodness of probiotics is small and limiting and non-conclusive and devoid of any strong evidences. Therefore, considering the popularity of probiotics, there is a need for large, high-quality, independent and vigorous studies like these to come to any general conclusions.

Source

1. David Schnadower et al. 2018, 'Lactobacillus rhamnosus GG versus Placebo for Acute Gastroenteritis in Children', *N Engl J Med.*, DOI: https://-doi.org/10.1056/NEJMoa1802598

2. Stephen B. Freedman et al. 2018, 'Multicenter Trial of a Combination Probiotic for Children with Gastroenteritis', *N Engl J Med.*, Vol. 379, DOI: https://doi.org/10.1056/NEJMoa1802597 ■

Organic Farming *Can Have Much Greater Implications* for Climate Change

Study shows growing food organically has higher impact on climate because of more land use

Organic food has become very popular in the last decade as consumers are becoming more aware and health and quality conscious. Organic food is produced naturally from organic farming which aims to increase the naturalness of food by minimizing chemical interference when producing it. So, organic food does not include any pesticides, synthetic fertilizers or other artificial additives. The produce of meat, eggs and other products from animals, is termed organic if animals were not subjected to any antibiotics or growth hormone supplements. Every food item produced organically is also more expensive than conventional food because without use of chemicals or additives, it takes longer time to produce organic food and thus requires more resources in terms of land, time etc. The demand for organic food is certainly higher and rapidly growing compared to the supply which is further contributing to high prices of organic food.

Conventional farming vs organic farming

Researchers at Chalmers University of Technology, Sweden developed a new methodology for analysing the impact of organic farming on climate via the factor of land-use by comparing conventional food production in agriculture


organic

with organic production. Their study showed that producing organic food contributed to higher emissions into the environment. For example, organic peas farmed in Sweden had almost 50 percent higher impact on climate while for other foods like Swedish winter wheat this number was as high as 70 percent. This is attributed to two reasons; first, to the more land required for organic farming and second, since fertilizers are not used in organic farming the yields per hectare is considerably reduced. For every single food product, be it organic meat or dairy product the land required is much more for organic production compared to conventional farming. This greater land use automatically leads to higher carbon dioxide (CO2) emissions because for every land which needs to be cultivated, forests are converted by cutting trees leading to deforestation. Deforestation accounts for 15 percent of total greenhouse emissions on our planet. Simply put, felling of trees is doing an irreversible damage to the environment and to the ecosystem (flora and fauna).

'Carbon opportunity Cost'

In their study published in *Nature*, researchers used a new metric called 'Carbon opportunity Cost' for the first time which evaluates the carbon footprint through effects of higher land use and how it contributed to CO2 emissions from deforestation. So, CO2 emissions were charted against the total food yield in which the ratio of organic food certainly lagged. The amount of carbon stored in forests was taken into account and as a result of deforestation CO2 is released into the atmosphere. Surprisingly, land use factor and its effect on CO2 emissions has never been analyzed before in any previous study perhaps due to lack of straightforward and easily applicable methods. The new metric 'Carbon opportunity Cost' allows for a simple yet detailed comparison. Total production in the country and total yields per hectare for organic and conventional farming statistics were provided by Swedish Board of Agriculture.

Organic farming never uses artificial fertilizers as the crops are nourished and nurtured through nutrients naturally present in the soil and if needed only natural pesticides are used. The flipside is that valuable resources like land, water and energy consumed are much higher in organic farming and its relevant to understand how it can be made sustainable over a period of time. According to this study consuming organically produced beans or chicken is better for the climate then let's say conventionally produced beef. And eating pork, chicken, fish or eggs will have lower impact on environment than say eating beef or lamb.

However, this study does have limitations – as it was restricted to a few crops and in only one region of a country. So, the recommendation is not to stop consuming organic food altogether. But it is clear, where impact on climate is concerned, organic food fares worse than conventional food because of the farming methods. There is still lack of substantial scientific evidence to show that organic food is more health friendly or even environment friendly than conventionally farmed food.

Key points

- Organic food is more expensive than conventional food because it is grown without any chemicals or additives and so it takes longer time to produce it requiring more resources in terms of land, time etc.
- Study in Sweden shows that producing organic food contributed to higher emissions into the environment because of comparatively more land use.

So even if one assumes organic food is better for people, it may not be so good for the planet! More data is certainly needed to arrive to generalized conclusions. The analysis in this study could also be correlated to biofuels as their production also needs larger land area compared to conventional fuels.

Source

Timothy D. Searchinger, Stefan Wirsenius, Tim Beringer, Patrice Dumas 2018, 'Assessing the efficiency of changes in land use for mitigating climate change', *Nature*, Vol. 564, no.7735, DOI: http://dx.doi.org/10.1038/s41586-018-0757-z ■

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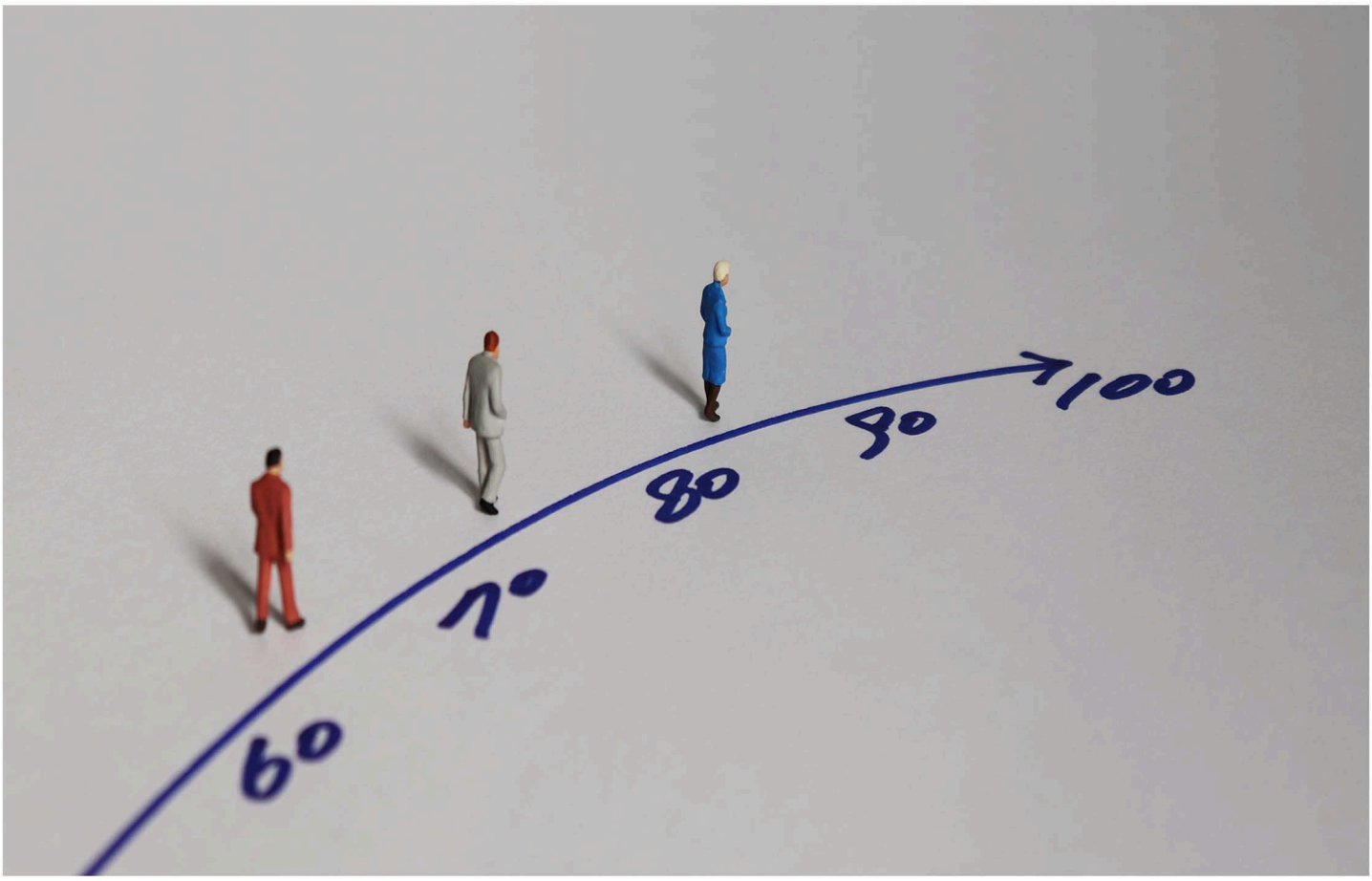
New Anti-Ageing *Intervention to* Slow Motor Aging *and Prolong Longevity*

Study highlights the key genes which can prevent motor function decline as an organism ages, for now in worms

Ageing is a natural and inevitable process for every organism in which there is a decline in function of many different organs and tissues. There is no cure for ageing. Scientists are exploring the process of ageing and any sighting of how it could be slowed down is of intrigue to everyone.

As animals and humans age, there is gradual yet significant deterioration in motor functions due to changes in the neuromuscular system – example reduced muscle strength, power of limb muscles etc. This decline which generally starts around midlife is the most prominent feature of ageing and is responsible for most of the problems faced by elderly which impacts their independent living. To be able to stop or even slow down the decline in motor functions is the most challenging aspect for study of anti-ageing and brings focus onto the basic functional unit of the neuromuscular system called the 'motor unit' i.e. the point where motor nerve and muscle fiber meet.

Researchers from University of Michigan Life Sciences Institute USA have revealed the main underlying cause of progressive decline in motor function which was responsible for increasing frailty in tiny ageing worms. More so, they have discovered a way to slow down this decline. In their study published in *Science Advances*, they have identified a molecule which can be the right target to improve motor function. And this particular pathway in worms could be indicative of



of something similar in ageing mammals as well including humans. Millimeter-long roundworms called nematodes (*C. elegans*) exhibit a pattern of ageing very similar to other animals though they survive only for about three weeks. But this limited life span makes them an ideally suited model system to study the scientific processes behind ageing as their lifespan can be easily monitored over a short duration of time.

Important component of ageing

When worms age, they start to gradually lose their physiological functions. When they reach middle of their adulthood their motor skills start showing decline. Researchers wanted to look at the exact reason for this decline. They set out to understand the change in the interaction of cells as worms were ageing and analyzed the positions where motor neurons communicated with the muscle tissue. A gene (and related protein) was identified called SLO-1 (slowpoke potassium channel family member 1) which has a key role in regulation of these communications by acting as a regulator. SLO-1 acts at neuromuscular junctions and dampens the activity of neurons which in turn decelerates the signals from motor neurons to the muscle tissue and thus reduces the motor function.

Researchers manipulated SLO-1 by using standard genetic tools and also a drug named paxilline. In both these scenario, two significant effects were seen in roundworms. First, worms maintained a better motor function and second, their lifespan increased as compared to normal roundworms. So, it was like having a longer life span but also with improved health and strength as both these parameters got enhanced. Timing was key for these interventions. Manipulations to SLO-1 when done very early in the worm's life span had no consequence, and in very young worms it had an opposite quite detrimental effect. The intervention works the best when done in middle adulthood. Researchers now

want to understand the role of SLO-1 in early development in roundworms. This can help to gain insights into the underlying mechanisms of ageing because such genetic and pharmacological interventions can help in promoting health as well as longevity.

Though this study is limited to worms, SLO-1 is conserved across many animal species and thus this discovery could be applicable to understanding ageing in other model organisms as well. However, it's not straightforward to study ageing in higher organisms due to longer duration of life span. That is why experiments need to be conducted in other model organisms apart from worms like yeast, Drosophila and mammals like mice whose lifespan is maximum 4 years. Experiments could then be conducted on human cell lines as doing it in vivo in humans is impossible. Continuous experiments would be needed to unravel molecular and genetic mechanisms behind ageing. This study has provided immense knowledge about a molecular target, potential site and the exact timing at which the anti-ageing strategy should be applied. The study accepts the inevitability of motor decline yet inspires to overcome it by preventing early cognitive and motor decline.

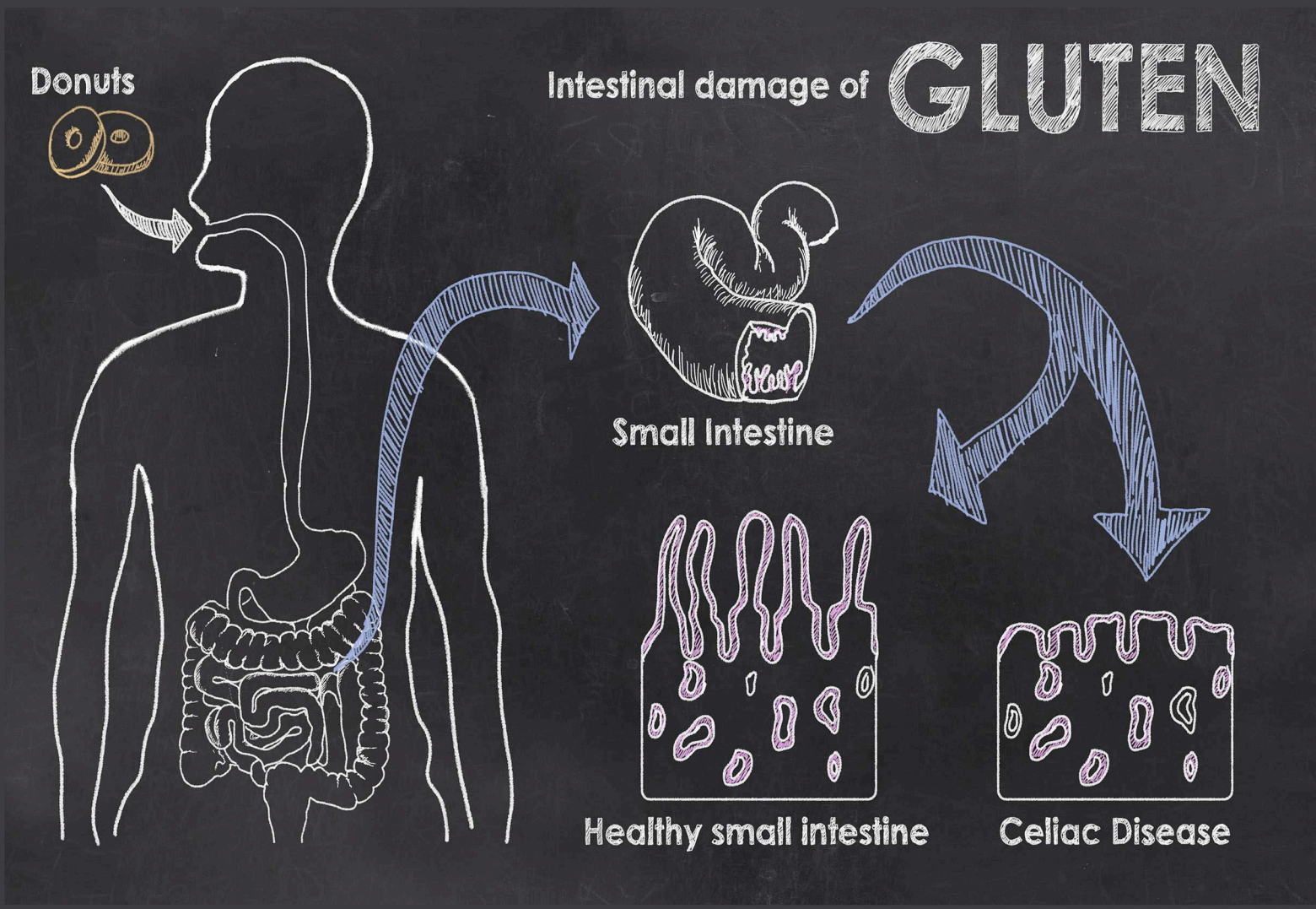
Source

Guang Li et al. 2019, 'Genetic and pharmacological interventions in the aging motor nervous system slow motor aging and extend life span in C. elegans', *Science Advances*, DOI: https://doi.org/10.1126/sciadv.aau5041 ■

Gluten Intolerance: *A Promising Step Towards Developing a* Treatment for Cystic Fibrosis and Celiac *Disease*

Study suggests a new protein involved in development of gluten intolerance

Almost 1 out of 100 people suffer from celiac disease, a common genetic disorder which could sometimes also be triggered by environmental factors and diet. People suffering from celiac disease develop a sensitivity to gluten – found in wheat, rye and barley. This disease is a severe autoimmune disorder of our intestine in which our immune system triggers a response against our body's own cells - hence the 'autoimmunity' – when any food containing gluten is consumed. This negative response by our immune system damages the surface of small intestine. Initially celiac disease was found in countries with higher Caucasian population, now its also being reported in populations. There is unfortunately no cure available for celiac disease and patients' need to keep a strict watch on their diet which is the only therapy available.


Donuts
Intestinal damage of GLUTEN
Small Intestine
Healthy small intestine
Celiac Disease

Association between celiac disease and cystic fibrosis

Celiac disease also occurs higher (by almost three times) in people who suffer from cystic fibrosis as there is a definite co-occurrence between these two diseases. In cystic fibrosis, thick and sticky mucus builds up in the lungs and intestine mainly caused by mutations in the gene for protein CFTR (cystic fibrosis transmembrane conductance regulator). CFTR protein plays a central role in keeping the mucus fluidic. So, when this ion transport protein is not generated, mucus starts to clog up and this malfunction also triggers other problematic reactions in the lungs, intestines and other organs mainly due to the immune system getting activated. These reactions or effects are very similar to what is triggered by gluten in celiac disease patients. That is why it is being understood that these two disorders are linked.

Researchers from Italy and France set out to understand the nature of connection between celiac disease and cystic fibrosis at the molecular level in their study published in *The EMBO Journal*. Since gluten is very difficult to digest, its longer protein parts enter the intestine. Researchers used human intestinal cell lines in the laboratory which are sensitive to gluten. It was seen that one particular protein part (or peptide) called P31-43 is able to directly bind to CFTR and impair its function. And once function of CFTR is hindered, cellular stress and inflammation gets triggered. Researchers concluded that CFTR is crucial in mediating gluten sensitivity in celiac patients.

One particular compound called VX-770 could inhibit the interaction between the peptide P31-43 and CFTR protein by blocking the active site on the target protein. So, when human intestinal cells or tissues which were collected from celiac patients were pre-incubated with VX-770, the interaction between the added peptide and the protein did not take place and thus immune reaction was not elicited at all. This marks VX-770 as essential for protecting gluten-sensitive epithelial cells from the bad effects of gluten consumption. In gluten sensitive mice, VX-771 provides protection from gluten-induced intestinal symptoms.

Key points

- **There is no cure available for celiac disease in which patients develop a sensitivity to gluten.**
- **Researchers studied the nature of connection between celiac disease and cystic fibrosis at the molecular level.**
- **The developed a treatment for cystic fibrosis which may also be a starting point for developing a potential treatments for celiac disease.**

This study is a promising first step towards developing a treatment via inhibitors of protein CFTR which can treat cystic fibrosis and may also be a starting point for developing a potential treatment for celiac disease. More clinical trials are needed to analyze the dose and administration of the potential CFTR inhibitors. Results could help patients who have gluten intolerance to be able to use medication without changing or restricting their diet.

Source

Valeria R Villella et al. 2018, 'A pathogenic role for cystic fibrosis transmembrane conductance regulator in celiac disease', *The EMBO Journal*, DOI: https://doi.org/10.15252/embj.2018100101 ■

Intermittent Fasting *Can Make Us Healthier*

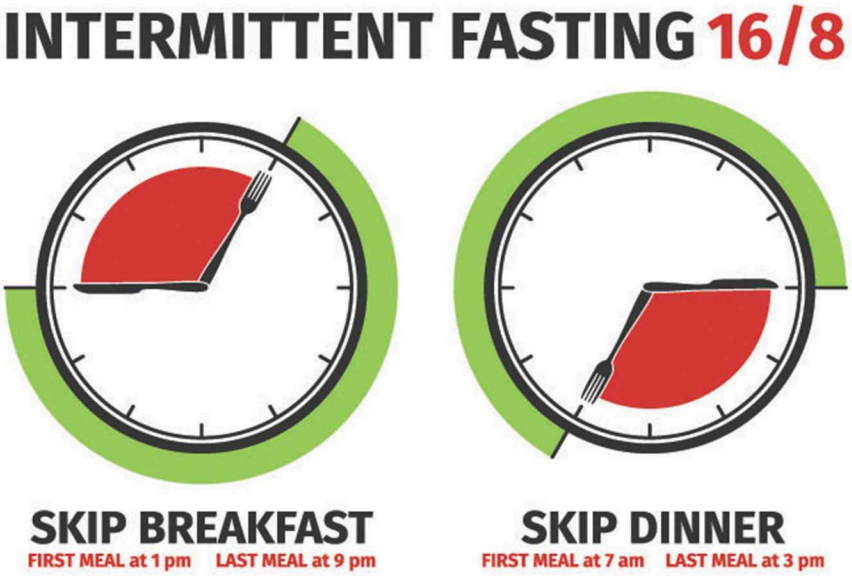
Study shows that intermittent fasting for certain intervals can promote good health by boosting our metabolism

Fasting is a natural phenomenon in most animals and to accommodate fasting in dire circumstances, metabolic changes occur in their body. Fasting allows the body to burn excess fat inside. So, it's considered a very normal and natural process which doesn't have any detrimental effects on our body system as during fasting 'body fat' - food energy stored in the body - is consumed. Intermittent fasting involves eating during a specific time frame and then fasting for certain extended periods of time. Intermittent fasting is a diet which has become popular as it is thought to have immense weight loss benefits and it is now labelled as a lifestyle choice. Though it is strongly believed that intermittent fasting is beneficial, there is less clarity on the exact nature of these benefits.

When we eat food, food is ingested and then some of it is stored for energy which can be used later. The hormone insulin is primarily responsible for this process. The excess energy is stored in the liver as sugars called glycogens, here the storage capacity is very limited. Once this limit times out, our liver starts to convert excess sugars into fat. All of this excess fat cannot be stored in the liver because of storage limitation; hence it is exported to other parts of the body where the storage is unlimited. This excessive storage of fat then becomes the reason for weight gain and other diseases.

Effect of fasting on our circadian clock

Researchers from University of California Irvine, USA have investigated the impact of fasting on our body and more specifically on our circadian clock. Circadian rhythms are our daily sleep-wake cycles which are integral to life and maintain our body's equilibrium. This 24-hour cycle not just controls our sleep and wake pattern but also involves metabolic, physiological and behavioral changes which affect every living tissue in our body. For example, when we are deprived of glucose, liver starts creating ketones from fatty acids so that body could use that as an emergency energy source.



The food which we consume has a major effect on our circadian clock as eating modulates circadian rhythms, what is still not understood is how exactly does 'fasting' impact these rhythms and in turn affect our health. Researchers set out to understand how fasting can influence circadian rhythms in liver and skeletal muscles in mice in their study published in Cell Reports. The animals were on a 24-hour fasting period, when their physiological functions were measured. When mice were fasting, they used less oxygen and energy. But as soon as they started eating again, this physiological change is reversed. Fasting caused fasting-sensitive cellular responses in mice which led to reorganization of genes in skeletal muscle and liver, causing their metabolism to speed up and this promoted good health. Different muscles showed varied response, example skeletal muscles were twice responsive to fasting compared to liver muscles. These gene changes were clear 'during' fasting. Thus, fasting influences the circadian clock as the animal's circadian oscillations were more robust in fasting mice. Also, when compared, despite consuming same amount of energy, fasting mice did not develop obesity or metabolic disorders as the other mice.

Exercise, protein-rich diet and intermittent fasting

The findings suggest that fasting basically reprograms different cellular responses. And if timing of fasting could be planned in an efficient manner, there could be a positive effect on cellular functions and this could provide health benefits and protection against ageing-related diseases. It is clear that fasting is enabling new rhythmic gene expression (by regulation) and could drive changes in our metabolism via our circadian clocks. This can have an overall positive impact on our health. It's well established that disruption in circadian rhythms can increase risk of obesity and also metabolic disorders like diabetes, which is further validated by the current study on fasting. Findings define only the first step in understanding how fasting influences our circadian rhythms, but it's in the direction of how to find the most optimal fasting regime/guidelines which can have metabolism-boosting effects and can promote good health. Along with exercise and protein-rich diet, intermittent fasting (staring with a 12-hour interval) can be a good lifestyle addition.

Source

Kenichiro Kinouchi et al. 2018, 'Fasting Imparts a Switch to Alternative Daily Pathways in Liver and Muscle,' *Cell Reports,* Vol. 25, no.12, DOI: https://-doi.org/10.1016/j.celrep.2018.11.077 ■

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Air Pollution A Major Health Risk to the Planet: *India Worst Affected Globally*

Comprehensive study on the seventh biggest country of the world, India, shows how ambient air pollution is majorly affecting health outcomes

According to WHO, ambient air pollution is responsible for almost 7 million annual deaths worldwide due to exposure to fine particles in the polluted air. Ambient or outdoor air pollution is estimated to cause deaths in the range of 15-25 percent due to lung cancer, chronic pulmonary disease, heart diseases, stroke, severe asthma and other respiratory ailments including pneumonia. In just less than a decade, air pollution has become a major disease burden for our planet as it prominently sits among the top 10 killers. Indoor pollution via use of wood, charcoal, dung, and crop residue as solid cooking fuel and outdoor pollution caused by particulate matter is now a major global environmental and health problem. This burden is disproportionately higher in low- and middle-income countries than in high-income countries. There are several reasons including rapid urban expansion, less investment into cleaner sources of energy and pressure for economic growth. Also, prevailing winds and climactic events are now carrying pollutants to developed parts of the world like USA as our atmosphere connects all distant regions of the planet. This marks air pollution as a grave global concern.

Steady increase in air pollution across the country

A comprehensive study in


WARNING
N95

The Lancet Planetary Health shows a first of its kind inclusive report on estimate of deaths, burden of disease and reduced life expectancy in association with air pollution across every region of seventh largest country of the world, India – a low-to-middle-income country as designated by the World Bank. The study reports that one in every eight deaths in India in the year 2017 was due to air pollution of pupils less than 70 years of age, the total number of deaths being 1.24 million. Both ambient as well as household pollution are one of the biggest factors for disability and death, more than tobacco or high blood pressure or high salt intake even. India, a fast-growing country is the second most populous country in the world and its population now stands as 18 percent of total world population. India has a disproportionally high percentage of disease burden and mortality- about 26 percent - of worldwide premature deaths caused by air pollution.

India's annual average level of fine particles in air, commonly called PM 2.5 was 90 was 90 µg/m3--the fourth highest in the world and more than twice the limit of 40 µg/m^3 recommended by the National Ambient Air Quality Standards in India and nine times over the WHO annual limit of 10 µg/m3. The minimum levels of exposure of PM 25 was between 2.5 and 5.9 µg/m3 and almost 77 percent of India' population was exposed and unprotected to ambient air pollution limits above the national safe limits. Coarse particles are of lesser concern because they only cause irritation in eye, nose and throat. Fine particles (PM 2.5) are most dangerous and small enough to venture deep into lungs when breathing and they even might enter one's bloodstream creating havoc on our lungs and heart and causing irreversible damage.

Region wise analysis

29 states of India were divided into three groups based on social development index (SDI) which is calculated using per capita income, education levels and fertility rates. The state wise distribution highlighted significant variation among regions. The worst affected regions were many states that were poor, less developed like northern states of Uttar Pradesh, Rajasthan, Bihar, Jharkhand which have lower SDI. If air pollution was well below national limits, the average life expectancy in these states would increase by at least two years. Interestingly, affluent states like Delhi, Punjab, Haryana and Uttarakhand also ranked poorly and were among worst affected and life expectancy in these states could also increase from between 1.6 to 2.1 years if air pollution is controlled. The pan country average life expectancy was evaluated to be at least 1.7 years higher if air pollution was causing minimal health loss. In the past decades there has been a decline in household pollution as usage of solid fuel for cooking is now steadily decreasing in rural India due to increased availability of clean cooking fuel, however strong sustenance is this area is a must.

Key points

- **Air pollution is a grave global concern affecting millions of lives worldwide.**
- **A first inclusive report has been published which includes estimate of deaths, burden of disease and reduced life expectancy in association with air pollution across every region of seventh largest country of the world, India.**

This study is the first comprehensive study on the impact of air pollution for a country highlighting the ground reality and detrimental aspects of air pollution. The study was carried out by 40 experts across the nation led by India-State-Level Disease Initiative of the Indian Council of Medical Research, Public health foundation of India, Institute of Health Metrics and evaluation in collaboration of Ministry of health and family welfare, Government of India. Systematic efforts are necessary to address various sources of air pollution in India including-transport vehicles, constriction, industrial emission from thermal plants etc., use of solid fuels in residential or commercials, agriculture waste burning and diesel generators. Such efforts require region wise reference points for improving the situation and these reference points can be based on the robust estimates of health impact made in this study. It can be a useful guide to mitigate serious impact of air pollution in India and could also help us to gain perspectives for other low-income and middle-income countries. Different initiatives and strategies need to be devised by increasing community awareness and reforming polices.

Source

India State-Level Disease Burden Initiative Air Pollution Collaborators, 'The impact of air pollution on deaths, disease burden, and life expectancy across the states of India: the Global Burden of Disease Study 2017', *The Lancet Planetary Health*, Vol. 3 No. 1, DOI: https://-doi.org/10.1016/S2542-5196(18)30261-4 ■

Discovery of Chemical Leads for Next Generation Anti-Malarial Drug

A new study has used robotic screening for shortlisting chemical compounds which could be 'prevent' malaria

According to WHO, there were 219 million cases of malaria worldwide and approximately 435,000 deaths in 2017. Malaria is an infectious disease caused by parasites *Plasmodium falciparum* or *Plasmodium vivax*. These parasites start their lifecycle when an infected mosquito transmits sporozoites into a human when it feeds on human blood. Some of these sporozoites cause an infection inside the human liver as they replicate. Subsequently, parasite bursts into red blood cells to start the infection. When blood gets infected, symptoms of malaria like chills, fever etc. appear in a person.

Currently available drugs for malaria generally appease symptoms of the disease 'after' the infection had occurred. They block replication of parasites in the human blood, however they cannot prevent transmission to new people via mosquitoes because the infection has already taken place. When an infected person gets bitten by a mosquito, the mosquito carries the infection to another person continuing the vicious cycle of infection. Unfortunately, malaria parasites are becoming resistant to most commercially available anti-malarial drugs. There is an urgent need for new anti-malarials which could not just treat symptoms but also prevent malaria infection from reaching the bloodstream so that it cannot be transferred to other people.

Targeting a new stage in parasite's lifecycle

In a new study published in Science, researchers have targeted the malaria parasite at its lifecycle's earlier stage – i.e. when the parasite first starts to infect the human liver. This is prior to the stage where the parasite starts replicating in the blood and causes infection to the person. Researchers took two years to extract malaria parasites from inside of thousands of mosquitos using modern

technology of robotics. For their study, they used *Plasmodium* berghei, a relative parasite which infects only mice. First, the mosquitoes were infected by the parasite, then sporozoites were extracted from these infected mosquitos – some of them were dried, frozen so not of any use. These sporozoites were then taken to the drug screening facility where potential drugs/inhibitors/chemical compounds were tested for their effect. In one round about 20,000 compounds could be tested by using a robotic technology and sound waves wherein minute amounts of each chemical compound were added i.e. one compound added per every sporozoite cell. Each compound's capability to kill the parasite or even block its replication was evaluated. The compounds which were toxic to liver cells were eliminated from the list. Testing was done for the same set of compounds on other *Plasmodium* species as well and also on other life-cycle stages apart from liver stage.

Chemical leads identified

A total of more than 500,000 chemical compounds were tested for their capability to stop the parasite when it's at the human liver stage. After many rounds of testing, 631 compounds were shortlisted which were seen to block malaria infection before symptoms began so potentially preventing

transmission into blood, new mosquitoes and new people. 58 among these 631 compounds even blocked the parasite's energy-generating process in the mitochondria.

This study could be the foundation for developing next generation novel 'malaria prevention' drugs. The research has been carried out in the open-source community which allows other research groups around the globe to freely use this information to further their work. Researchers want to test the 631 promising drug candidates to analyse their effectiveness and these compounds will also need to be checked for their safety for human consumption. Malaria urgently needs a novel drug which is affordable and can be delivered to any part of the world without additional demands of infrastructure, healthcare personnel or other resources.

Source

Yevgeniya Antonova-Koch 2018, 'Open-source discovery of chemical leads for next-generation chemoprotective antimalarials', Science, Vol. 362, no.6419, DOI: https://doi.org/10.1126/-science.aat9446

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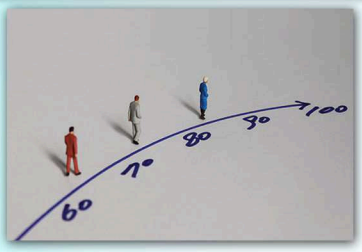
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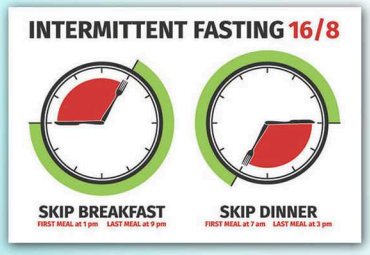
INTERMITTENT FASTING 16/8
SKIP BREAKFAST
FIRST MEAL at 1 pm LAST MEAL at 9 pm
SKIP DINNER
FIRST MEAL at 7 am LAST MEAL at 3 pm


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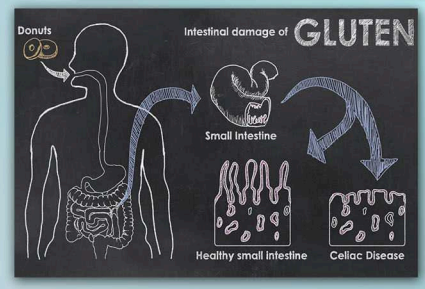
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Intestinal damage of GLUTEN
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