Staying alert thanks to food

A decades-long study has found that colourful meals may brighten our later years

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Outside the usual advice to exercise, get enough sleep and stay mentally active, a study that lasted over two decades pinpoints items in the diet that would help us stay alert as we age.

Tian-Shin Yeh, Changzheng Yuan, Alberto Ascherio, Bernard Rosner, Walter Willett, Deborah Blacker, from Harvard University in the United States and Zhejiang University, Hangzhou, China, describe the details of the study in a paper in *Neurology*, the medical journal of the American Academy of Neurology. "Our results are exciting because they show that making simple changes to your diet could help prevent cognitive decline," says Willett, one of the authors.

With the number of older persons in the world's age profile rising fast, dealing with age-related loss of cognition, or the ability to remember, reason, learn, would become a major public health issue, the paper observes. And, as there is no known remedy, it is important to look for preventive strategies.

While changes in the brain that result in cognitive decline, or dementia, may start long before effects are clinically apparent, an early warning could be subjective cognitive decline, or SCD, where cognitive decline is self-perceived. Measures that are found to defer the onset of SCD could hence be effective in putting off more serious manifestations, the paper says.

The paper then refers to flavonoids, a group of compounds found in many fruits and vegetables, which are believed to be powerful antioxidants. The cells of living things contain sources of reactive oxygen to promote and regulate processes, like cell signaling or maintaining temperature or fluid balance. When these agents, which are called free radicals, are there in excess, however, the result is cell damage, including DNA damage. Hence the value of antioxidants, which can neutralise free radicals. As oxidative stress has been considered to have a role in age-related cognitive decline, it has been proposed, the paper says, that flavonoids may help retard the loss of cognitive function.

Whether this belief is a fact, however, has not been established, the paper says. Some short-term trials have provided evidence of flavonoids being effective, but there is nothing conclusive, particularly in respect of the different flavonoid substances contained in different items of food. On the contrary, it is found that flavonoids in the diet are not well absorbed in the human body. And that the rise in antioxidant potential of the blood after consumption of flavonoids is not really a result of the flavonoids.

The team of researchers hence undertook the study, over a 20-year period, of monitoring the dietary practices of two large groups of men and women, followed by an assessment of SCD by the participants themselves, to see if there was a relationship of a flavonoid-rich diet with subsequent subjective cognitive decline.

FLAVONOIDS

Flavonoids are substances produced almost entirely by plants and can be made out in the yellow or red/blue colours of petals, with the function of attracting pollinators. But flavonoids have other functions in plants, and they include processing components of sunlight, helping organisms to prepare nitrogen in the air for absorption by the plant and protection from pathogens. As flavonoids are there in almost all plant varieties, and, unlike some substances like alkaloids, they do not harm animals, flavonoids are a part of the diet of many animals, including humans. Over 5,000 flavonoids have been identified and are classified, based on chemical structure. The table shows some of the groups of flavonoids and foods that are the best sources.

Flavonoids	Food Sources
Simple Flavonoids	
Flavan-3-ols	Green tea, chocolate, tree fruits, grapes, red wine
Flavanones	Citrus fruits and juices
Flavones	Parsley, celery seed, oregano
Flavonols	Onions, apples, tea, berries
Anthocyanidins	Most berries, stone fruits
Complex Flavonoids	
Condensed Tannins (Proanthocyanidins)	Chocolate, stone fruit (apples, pears), grapes, strawberries, cranberries, nut skins, cinnamon, beer, wine, barley, legumes

The first part of the study began in 1976, with 1,21,701 female nurses registered in the U S. The study design was through questionnaires and the strength of the study is the regularity and the long period covered. Every second year, the participants filled in a questionnaire that detailed their medical history, potential risk factors and newly diagnosed diseases. And in 1980, 1984, 1986, and thereafter, every four years, they filled in a questionnaire that detailed the content and frequency of food they consumed. And again, starting from 2012, 49,693 women in the study responded to SCD questions, to watch for indicators of cognitive decline.

The other part of the study covered 51,529 male health professionals in the US, between 40 and 75 years of age. Information on lifestyle risk factors and medical history was collected every two years, and from 1986 the participants filled in the food habits questionnaire. The questionnaire, the paper says, is a recognised one, that has been successfully used in other studies as well.

The food-related questionnaires were filled in by the nurses till 2006 and by the health professionals till 2002, covering 20 years and 16 years respectively. The questions, which first covered 131 food items, were about how often the respondents consumed each food of a standard portion size in the previous year. And this led to data of the total flavonoids, flavonoids subclasses, other nutrients or foods consumed, and total energy intake, over the study period. The approach is said to reduce within-subject variation and best represents the long-term diet pattern. The part played by different flavonoid subclasses was then calculated from flavonoid content of each food and its consumption frequency. The focus was on the six most common flavonoids, as well as "total flavonoids", resulting in translation of the diet data into those of flavonoid intake.

The questionnaires relating to SCD were administered twice – 2012 and 2014 with the nurses and 2008 and 2012 with the health professionals. There were six yes-or-no questions to answer, to bring out whether the participants had experienced instances of forgetting things, getting confused, etc., to reveal if they had noticed SCD, aspects of cognitive decline in themselves, by around 2012.

The paper says that the subjective assessment of cognitive decline is reliable, as verified by records of persons who showed SCD and later developed clinical symptoms. The study also excluded cases where there were conflicting factors, leaving data of 49,493 women and 27,842 men,

RESULTS

The result of the questionnaires was that individuals who had noticed SCD, aspects of cognitive decline in themselves, by around 2012, could be identified, for comparison with the data of diet habits, recorded since 1986. The data has been divided into quintiles, or groups of 20 per cent, and it is found that the group with flavonoid intake in the top 20 per cent had a 20 per cent lower probability of developing SCD, than those in the lowest 20 per cent. The intake of the top 20 per cent was about 600 milligrams in a day, compared to 150 milligrams of the lowest group. And as for individual flavonoids, those found in some spices and yellow and orange fruits and vegetables, were found to lead to a 38 per cent reduction in the SCD risk.

The study also found that not only those who had a long-term diet of high flavonoids were benefitted, the benefits flowed even to those who had recently added flavonoids. It is interesting to see that even common foods, like tea and oranges, could make a difference, and with oranges, that the skin is richer in flavonoids than the pulp.

The study is a formal confirmation of the benefits generally associated with fruits and vegetables. A national programme to promote the correct diet may pay for itself by preventing losses, and costs, of cognitive decline of older persons.

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PLUS POINTS

Covid-19 & autoimmunity

The recent pandemic spread by the severe acute respiratory syndrome coronavirus 2 (Sars-CoV-2) is causing disease by mechanisms hitherto unknown. It is turning the immune system against the body itself, which is called autoimmunity. Normally, the body has multiple layers of defence against turning on itself. The Covid-19 virus, however, is noted for its exceptionality in causing autoimmune disease and rapidly declining health.

A crucial aspect of this disease pathophysiology has been brought to the forefront by Dr Anil Kumar Singh, a hospitalist affiliated with the Medicine Institute at Geisinger Clinic and clinical assistant professor of medicine at Geisinger Commonwealth School of Medicine, United States. Deriving from previous experience that autoimmune diseases can cause diverse multi-organ dysfunction, Dr Singh outlined the need to be aware about the associations. In an earlier pioneering investigation, he demonstrated the association between psoriasis, a blood disorder that manifests mainly as skin flaking, with significant renal disease.

Dr Singh gave insights into why one should be well rounded on the readiness about any angle associated with disease progression and evolution related to Covid-19. He drew attention to an important study involving a small subset of children who got severely affected with Covid-19. It is being appreciated that Covid-19 can cause a phenomenon called paediatric inflammatory multisystemic syndrome. The spectrum of this syndrome includes the features of the notorious Kawasaki disease and Kawasaki disease-shock syndrome. It is being seen that this condition may also occur in adult patients.

In West Bengal, several Kawasaki disease cases have also been reported during the ongoing Covid-19 pandemic. It has been long known that via molecular mimicry utilising pathogen associated molecular patterns, infections can be triggered for autoimmune and autoinflammatory diseases.

One of the major morbidity avenues for Covid-19 is heart inflammation and sudden heart attacks, also called acute coronary syndromes, or ACS. Dr. Singh raised the ominous concern that this heart inflammation can be caused by autoimmune mechanisms, resulting in myocarditis. It may be the cause of unanswered sudden deaths and points to the critical role of systemic steroids in the management of Covid-19 disease.

Antibody testing for Sars-CoV-2 may be needed to confirm previous Covid-19 infection as individuals with inflammatory multisystem disease may not have a current polymerase chain reaction or antigen test positivity. Such individuals may also have minimal respiratory symptoms, suggestive of this syndrome as a post-acute phenomenon. The involvement of a multi-disciplinary team early in the care of the patient is critical. This micro-inflammation may predispose to vascular injury and thrombosis, the procoagulant state escalating into cataclysmic outcomes including pulmonary embolism, ischemic stroke, mesenteric thrombosis and ACS.

Limited post-mortem pathologic examinations have demonstrated that Covid-19 spike glycoproteins localise with inflammation associated complement proteins like C4d and C5b-9 in the lungs and blood vessels of the skin. It becomes pertinent to evaluate for inflammatory markers in individuals who are presenting with fever or abdominal pain, vomiting, diarrhoea or rash of any kind. Such patients may often have elevated ferritin, which is an inflammatory marker in almost all hospitalised patients.

Though it takes anywhere between two weeks and several months for an autoimmune mechanism to kick in, it is intriguing how certain autoimmune conditions can occur almost immediately after infection by the Covid-19 virus in adult patients. They include Guillain-Barre syndrome, autoimmune hemolytic anemia and idiopathic thrombocytopenic purpura.

Next generation sequencing to understand the predisposition of which individuals will develop complex autoimmune sequelae is the need of the hour. Dr Singh felt the urgent need of pioneering in silico studies. They would help in finding out protein sequences in the virus that overlap with the body's proteins and can induce vasculitis-like diseases and toxic shock-like syndrome.

— Subhendu Maiti

COGNITIVE CATALYST

Swimming gives your brain a boost – but scientists don't know yet why it's better than other aerobic activities

SEENA MATHEW

It's no secret that aerobic exercise can help stave off some of the ravages of aging. But a growing body of research suggests that swimming might provide a unique boost to brain health.

Regular swimming has been shown to improve memory, cognitive function, immune response and mood. Swimming may also help repair damage from stress and forge new neural connections in the brain.

But scientists are still trying to unravel how and why swimming, in particular, produces these brain-enhancing effects. As a neurobiologist trained in brain physiology, fitness enthusiast and mom, I spend hours at the local pool during the summer. It's not unusual to see children gleefully splashing and swimming while their parents sunbathe at a distance — and I've been one of those parents observing from the poolside plenty of times. But if more adults recognised the cognitive and mental health benefits of swimming, they might be more inclined to jump in the pool alongside their kids.

New and improved brain cells and connections

Until the 1960s, scientists believed that the number of neurons and synaptic connections in the human brain were finite and that, once damaged, these brain cells could not be replaced. But that idea was debunked as researchers began to see ample evidence for the birth of neurons, or neurogenesis, in adult brains of humans and other animals.

Now, there is clear evidence that aerobic exercise can contribute to neurogenesis and play a key role in helping to reverse or repair damage to neurons and their connections in both mammals and fish.

Research shows that one of the key ways these changes occur in response to exercise is through increased levels of a protein called brain-derived neurotrophic factor. The neural plasticity, or ability of the brain to change, that this protein stimulates has been shown to boost cognitive function, including learning and memory.

Studies in people have found a strong relationship between concentrations of brain-derived neurotrophic factor circulating in the brain and an increase in the size of the hippocampus, the brain region responsible for learning and memory. Increased levels of brain-derived neurotrophic factor have also been shown to sharpen cognitive performance and to help reduce anxiety and depression. In contrast, researchers have observed mood disorders in patients with lower concentrations of brain-derived neurotrophic factor.

Aerobic exercise also promotes the release of specific chemical messengers called neurotransmitters. One of these is serotonin, which — when present at increased levels — is known to reduce depression and anxiety and improve mood.

In studies in fish, scientists have observed changes in genes responsible for increasing brain-derived neurotrophic factor levels as well as enhanced development of the dendritic spines — protrusions on the dendrites, or elongated portions of nerve cells — after eight weeks of exercise compared with controls. This complements studies in mammals where brain-derived neurotrophic factor is known to increase neuronal spine density. These changes have been shown to contribute to improved memory, mood and enhanced cognition in mammals. The greater spine density helps neurons build new connections and send more signals to other nerve cells. With the repetition of signals, connections can become stronger.

But what's special about swimming?

Researchers don't yet know what swimming's secret sauce might be. But they're getting closer to understanding it.

Swimming has long been recognised for its cardiovascular benefits. Because swimming involves all the major muscle groups, the heart has to work hard, which increases blood flow throughout the body. This leads to the creation of new blood vessels, a process called angiogenesis. The greater blood flow can also lead to a large release of endorphins — hormones that act as a natural pain reducer throughout the body. This surge brings about the sense of euphoria that often follows exercise.

Most of the research to understand how swimming affects the brain has been done in rats. Rats are a good lab model because of their genetic and anatomic similarity to humans.

In one study in rats, swimming was shown to stimulate brain pathways that suppress inflammation in the hippocampus and inhibit apoptosis, or cell death. The study also showed that swimming can help support neuron survival and reduce the cognitive impacts of aging. Although researchers do not yet have a way to visualise apoptosis and neuronal survival in people, they do observe similar cognitive outcomes.

One of the more enticing questions is how, specifically, swimming enhances short- and long-term memory. To pinpoint how long the beneficial effects may last, researchers trained rats to swim for 60 minutes daily for five days every week. The team then tested the rats' memory by having them swim through a radial arm water maze containing six arms, including one with a hidden platform.

Rats got six attempts to swim freely and find the hidden platform. After just seven days of training, researchers saw improvements in both short- and long-term memories, based on a reduction in the errors rats made each day. The researchers suggested that this boost in cognitive function could provide a basis for using swimming as a way to repair learning and memory damage caused by neuropsychiatric diseases in humans.

Although the leap from studies in rats to humans is substantial, research in people is producing similar results that suggest a clear cognitive benefit from swimming across all ages. For instance, in one study looking at the impact of swimming on mental acuity in the elderly, researchers concluded that swimmers had improved mental speed and attention compared with non-swimmers. However, this study is limited in its research design, since participants were not randomised and thus those who were swimmers prior to the study may have had an unfair edge.

Another study compared cognition between land-based athletes and swimmers in the young adult age range. While water immersion itself did not make a difference, the researchers found that 20 minutes of moderate-intensity breaststroke swimming improved cognitive function in both groups.

Kids get a boost from swimming too

The brain-enhancing benefits from swimming appear to also boost learning in children.

Another research group recently looked at the link between physical activity and how children learn new vocabulary words. Researchers taught children from age six-12 the names of unfamiliar objects. Then they tested their accuracy at recognising those words after doing three activities — colouring (resting activity), swimming (aerobic activity) and a CrossFit-like exercise (anaerobic activity) for three minutes.

They found that children's accuracy was much higher for words learned following swimming compared with colouring and CrossFit, which resulted in the same level of recall. This shows a clear cognitive benefit from swimming versus anaerobic exercise, though the study does not compare swimming with other aerobic exercises. These findings imply that swimming for even short periods of time is highly beneficial to young, developing brains.

The details of the time or laps required, the style of swim and what cognitive adaptations and pathways are activated by swimming are still being worked out. But neuroscientists are getting much closer to putting all the clues together.

For centuries, people have been in search of a fountain of youth. Swimming just might be the closest we can get.

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