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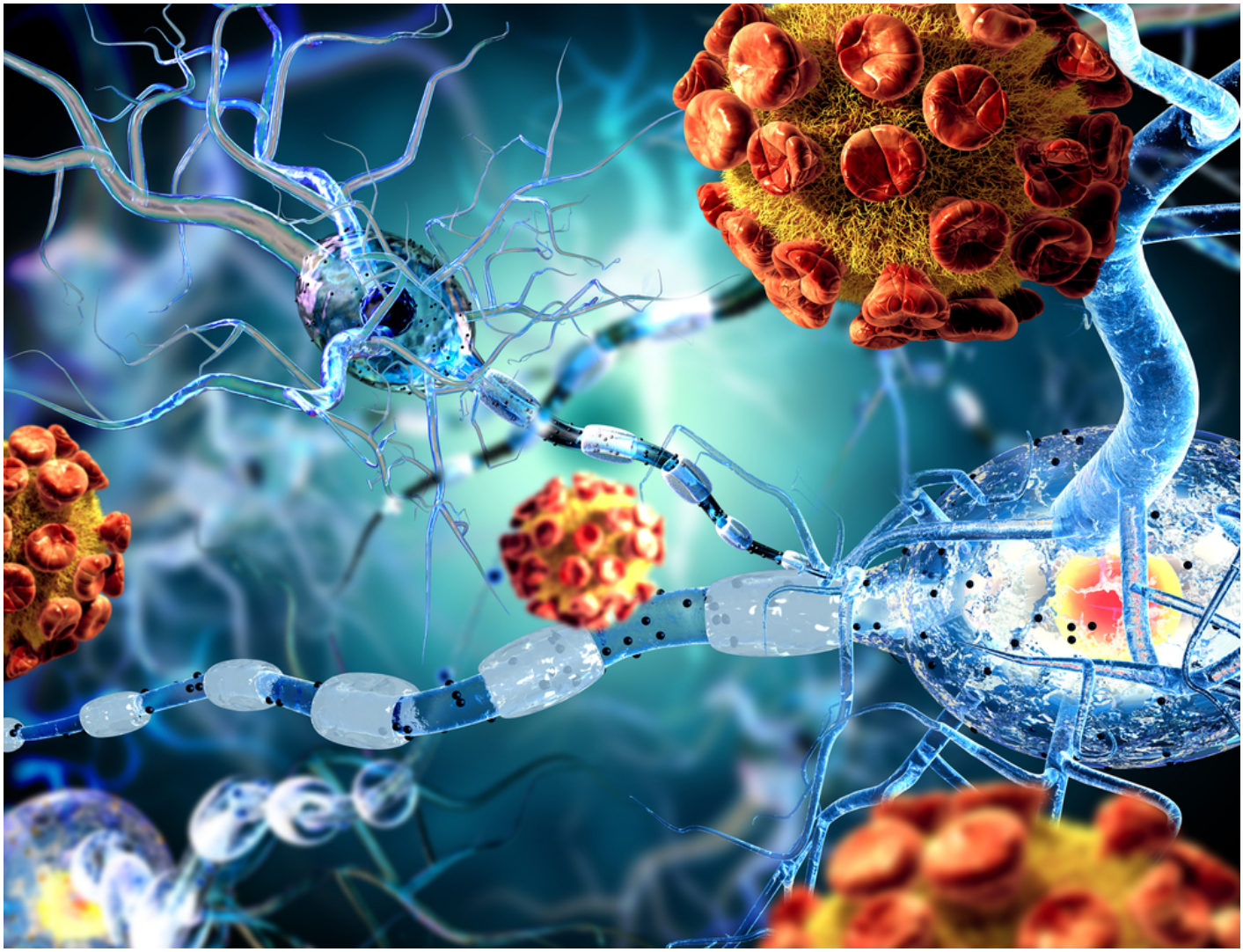

PREMIUM HEALTH VIEWPOINTS

Long COVID-Induced Neuropsychiatric Risks Can Last Beyond 2 Years; 1 Remedy to Protect From or Reverse the Situation

No previous study of COVID-19 cases has achieved such effective concurrent control

BY DR. YUHONG DONG AND MERCURA WANG TIME SEPTEMBER 12, 2022 PRINT

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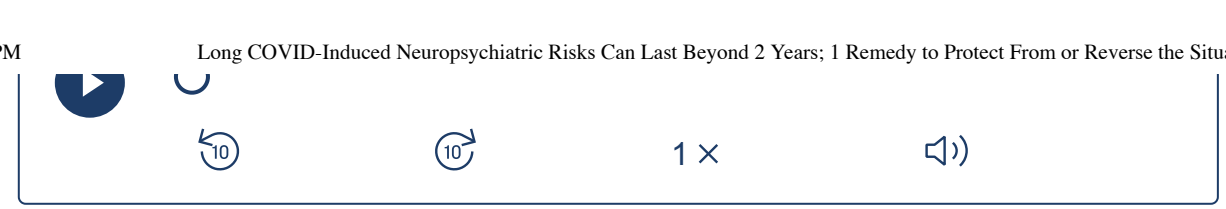


In this article, we examine the longest and largest study on COVID-19 neurological sequelae and the fundamental cause of COVID-19 injury to our nervous system. Targeting the root cause, we may potentially reverse the situation and potentially live longer.

The medical journal Lancet Psychiatry recently published a large-scale study of the neuropsychiatric sequelae of the COVID-19 infection.

A sequelae is a pathological condition resulting from a disease, or a secondary consequence or result of that disease.

This study is an analysis of retrospective cohort studies by seven scientists from Cambridge University and Oxford University in the United Kingdom, led by professor Paul Harrison, a psychiatrist at Oxford University.

The studies spanned four continents (with data collected from the United States, Australia, the UK, Spain, Bulgaria, India, Malaysia, and Taiwan) and 62 medical institutions. The studies were conducted over a period of two years and three months, from January 2020 to April 2022.

From the electronic medical records of approximately 89 million patients, the researchers identified more than 1.28 million cases of COVID-19 infection and matched them to a cohort of non-COVID patients who were suffering from other respiratory infections. That is, they matched exactly to the experimental group in terms of age, gender, occupation, risk factors for diseases, and vaccination status, during the same time period. There were more than 1.2 million patients each in the experimental and control groups.

No previous study of COVID-19 cases has achieved such a large and well-matched concurrent control group.

The analysis evaluated two-year time-varying hazard ratios for 14 neurological and psychiatric sequelae of COVID-19 infection. These disorders included:

- Brain fog, dementia, Parkinson's disease, and insomnia
- Anxiety disorders, mood disorders, and psychosis
- Epilepsy, encephalitis, intracranial hemorrhage, and ischemic stroke
- Guillain-Barré syndrome, neurological root and plexus disorders, and neuromuscular joint and muscle disorders

Of the 1,284,437 patients with the COVID-19 infection, their mean age was 42.5 years, ranging from children to the elderly.

Higher Mortality Risk in COVID Group Than Control Group

This analysis has provided us with very valuable information.

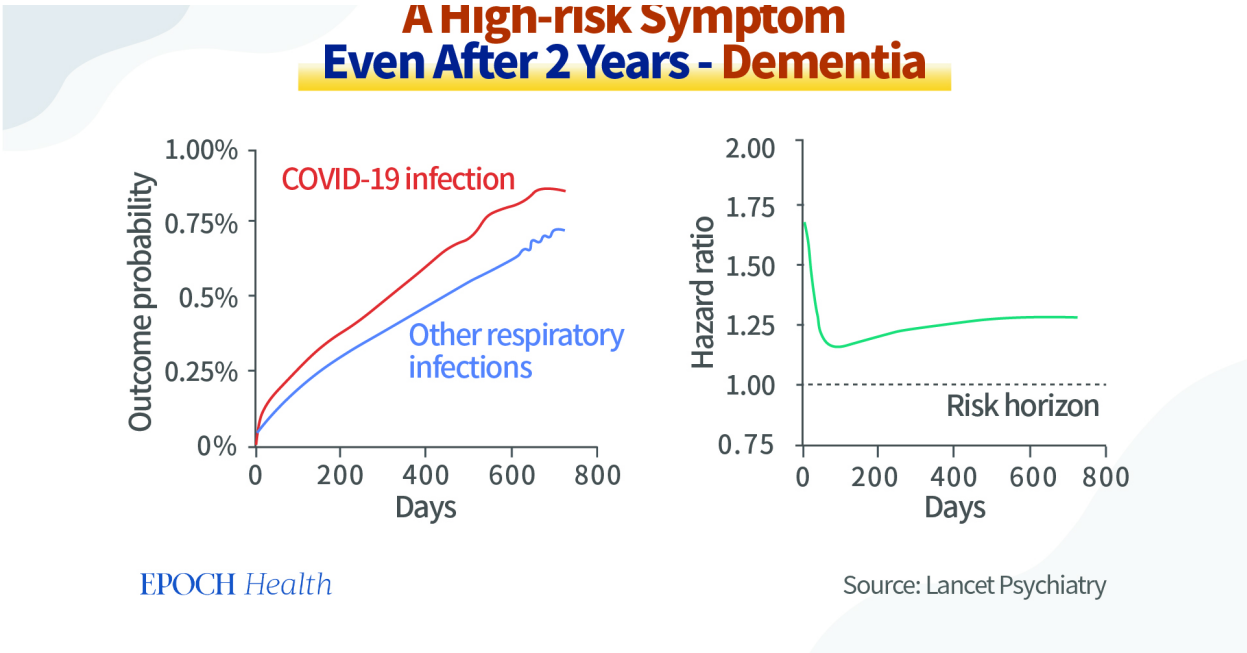
First, at six months after diagnosis, most of the 14 neurological and psychiatric disorders still had a significantly higher risk of morbidity among COVID patients than non-COVID patients.

Second, even at the end of the two-year follow-up period, the risk of cognitive deficits (i.e., brain fog), dementia, psychosis, Guillain-Barré syndrome, and epilepsy remained elevated, with far-reaching health consequences.

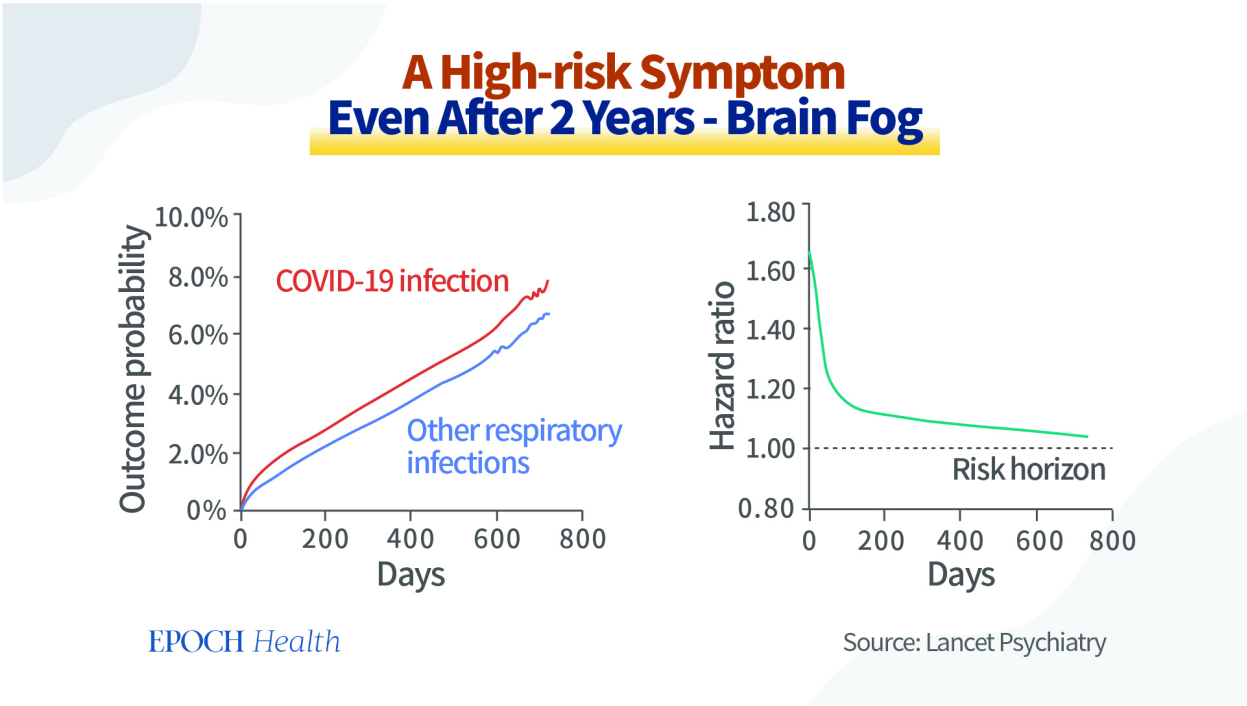
Let's use dementia, a typical symptom, as an example to explain the situation.

By comparing the cumulative incidence of dementia in the COVID-infected group and the group of patients with other respiratory infections (i.e., the control group), it was found that at six months of diagnosis, the risk of dementia was significantly higher in the first group than in the control group.

This risk remained higher in the first group than that of the control group at the end of the two-year follow-up period.



Another typical symptom is brain fog, whose hazard ratio remained higher than that of the control group at six months after diagnosis, as well as after two years.

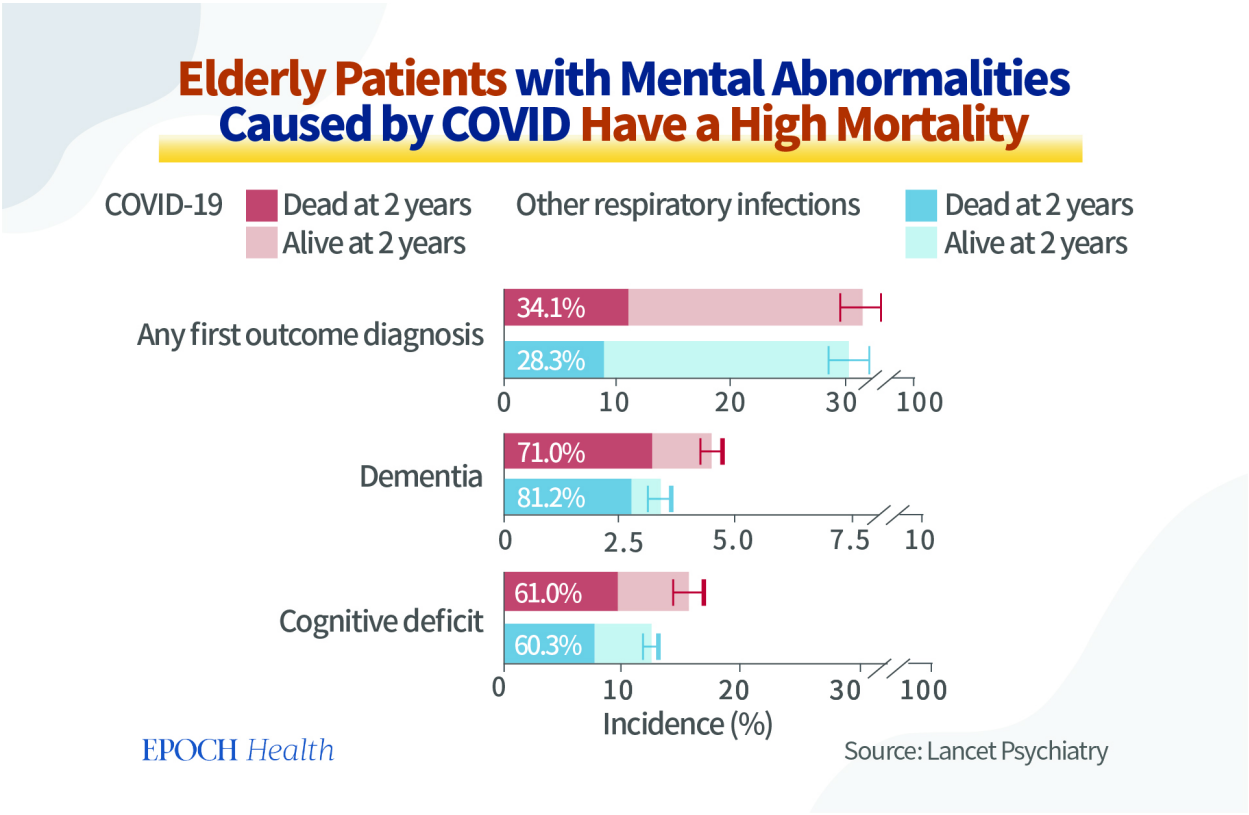


The risk of common mental abnormalities such as mood disorders and anxiety disorders recovered after one to two months.

The risk of psychosis, neuromuscular disorders, dementia, and brain fog is significantly higher in adults older than 65 years. The proportion of elderly patients who developed any of these neurological and psychiatric sequelae over two years was as high as approximately 32 percent, and the proportion of these

elderly patients who developed these neuro-psycho sequelae who died during the two-year follow-up was as high as 34.1 percent.

Of particular note, those older adults diagnosed with dementia, brain fog, or epilepsy had mortality rates of 71 percent, 61 percent, and 83 percent, respectively, over the two-year follow-up period.



It's obvious that the above information is a sign of serious illness. In other words, the occurrence of dementia and brain fog in the follow-up of these elderly patients portends a rather unfavorable prognosis for them.

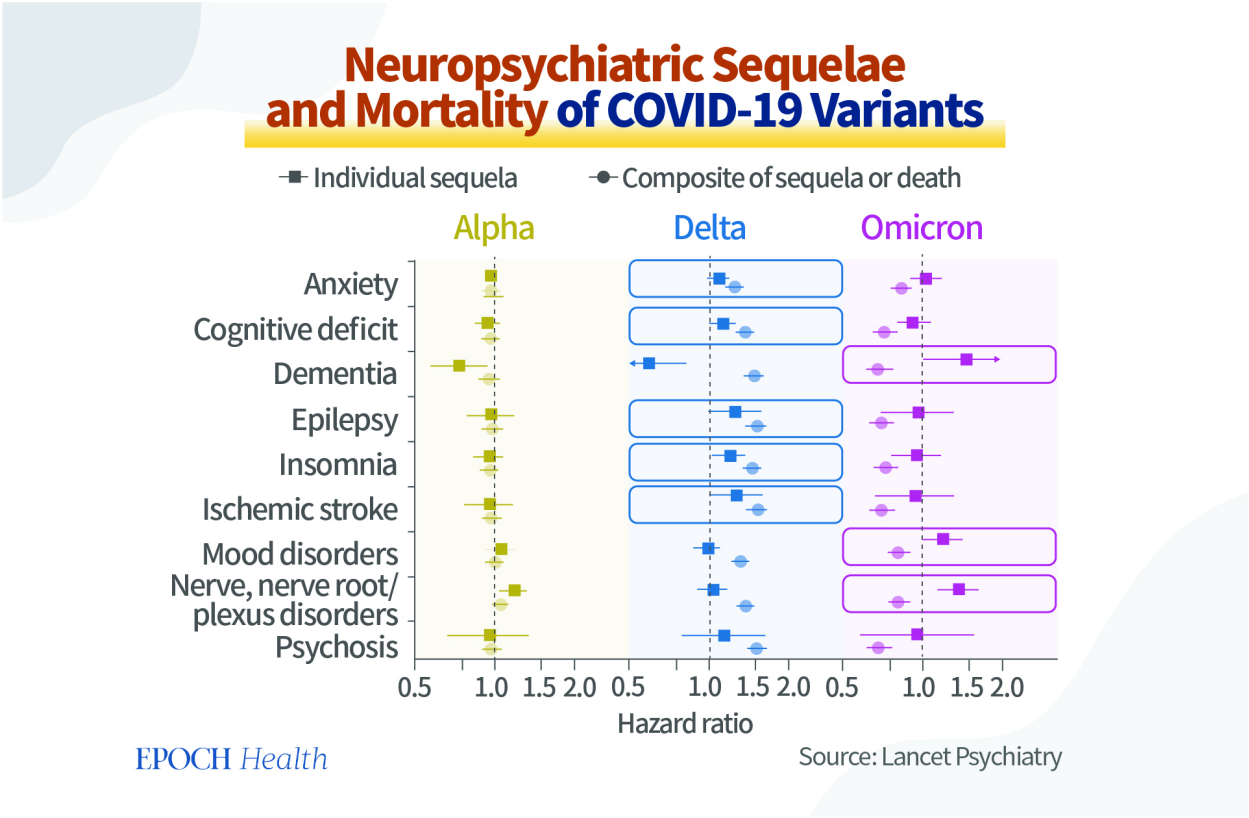
The Severity of Sequelae Varies Among Different Variants

In addition, the researchers had also analyzed information of different COVID-19 variants, including Alpha, Delta, and Omicron during the long follow-up period. This type of unique data has rarely been provided by other studies.

The Delta variant has significantly increased risks for majorities of both the incidence of neurological or psychological sequelae such as ischemic stroke, epilepsy, brain fog, insomnia, and anxiety, and patient mortality.

The Alpha variant has caused no change in either the incidence or mortality.

The incidence of several neuropsychiatric sequelae was significantly increased after Omicron variant infection, such as dementia, mood disorders, and neurogenic disorders. However, there was no increase in patient mortality.



Why Do Neuropsychiatric Impairments Persist for 2 Years After Infection?

From the above information, we can see that even two years after COVID-19 infection, the incidence of some neuropsychiatric sequelae was still persistently higher than that of the control group.

This is an indication that the SARS-CoV-2 virus is indeed different from other viruses as, on the neuropsychiatric aspect, once a patient is injured, it isn't easy for him or her to recover.

Research in this area is proliferating and has been a topic of interest to researchers for a long time.

According to two articles published separately this year, in the journals Science in January and Nature in July, the SARS-CoV-2 virus can directly or indirectly cause nerve cell damage. There are at least seven mechanisms through which the virus may affect the body's nerve cells long after acute infection.

1. It directly causes apoptosis of neuronal progenitor cells.

2. It attacks the blood vessels of the brain, causing ischemia and hypoxia. Endothelial diseases can lead to damage or fragility of the cerebral blood vessels, thrombotic events, or leaks.

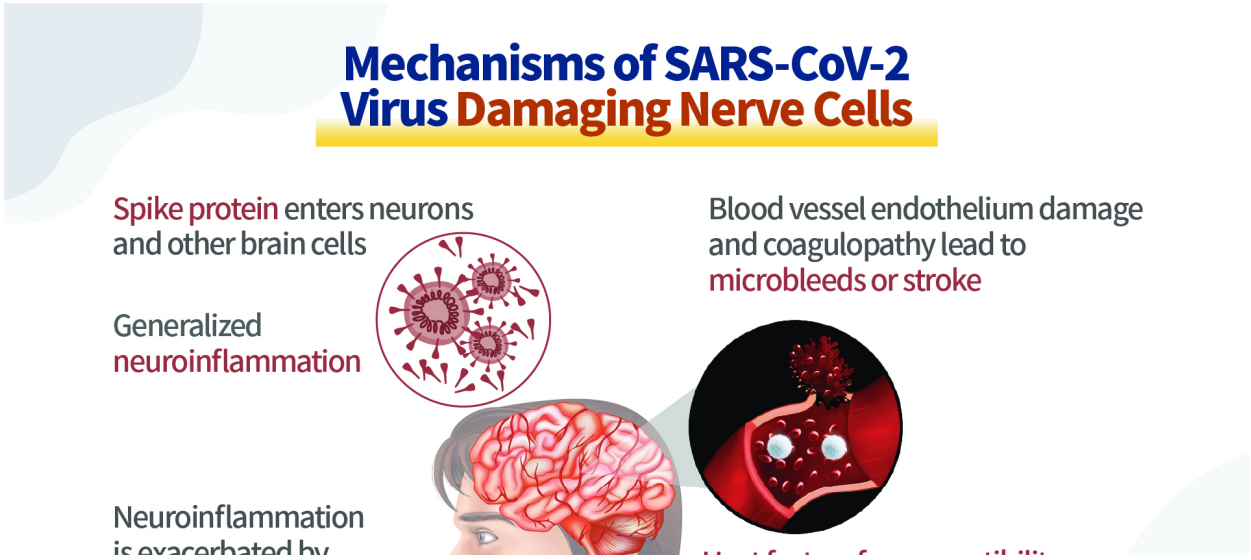
3. It causes autoimmune attacks. Autoimmunity not only attacks the virus, but may also attack the components of one's own neurons, including the outer protective layer of nerves (myelin), which has a similar function as the insulation skin of electrical wires. Once myelin is destroyed, our nerves won't be able to transmit neuronal signals as fast as we could. That's one of the reasons that we think, respond, and move more slowly.

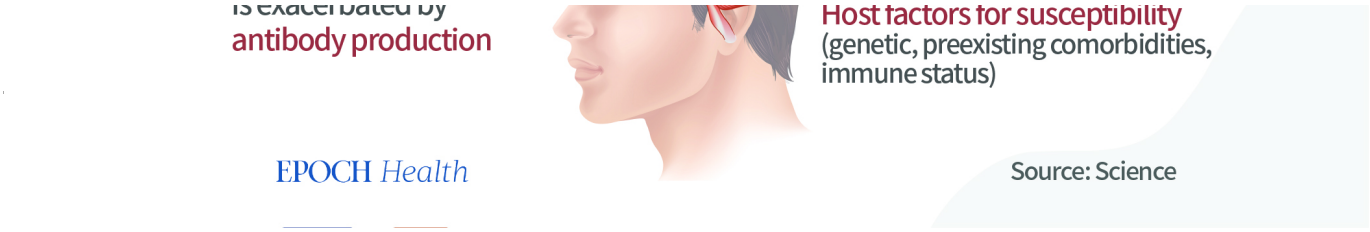
4. It causes the nervous system inflammation that induces injuries to our normal nerve cells.

5. It causes mitochondrial damage to nerve cells. The mitochondria are a cell's power plant. Once the mitochondria in nerve cells are damaged, the nerves lose their power supply and won't be able to function properly.

6. It impairs nerve cell lipid metabolism. Lipids account for 60 percent of the brain. Lipid disorders directly link to the dysfunction of the neuronal system.

7. It inhibits autophagic activity. Autophagy is a mechanism by which nerve cells renew themselves and remove waste. The autophagy process is like our internal waste recycling system. The inhibitory effects on autophagic process will cause more garbage to accumulate without an efficient garbage processing system, ultimately speeding up the aging process of brain cells.





It's evident that the impact of COVID-19 infection on the brain and nerves is multifaceted and comprehensive. This damage is far-reaching and long-lasting, and very difficult to recover from.

One phenomenon is worth noting. That is, the study mentioned that the incidence of mood disorders and anxiety in COVID-19 patients was transiently increased, suggesting that these symptoms might be caused by some transient triggers. The causes of such mood disorders and anxiety are different from the mechanism of normal neuron cell death and loss due to brain fog or dementia.

Mild COVID-19 Infections Can Also Alter the Brain

A study published in Nature in March found that even a mild COVID-19 infection can alter the brain.

In this study, Oxford University neuroscientists used UK Biobank's bio-specimens from nearly 800 participants, half of whom were COVID-infected and the other half were uninfected. Ninety-six percent of them weren't hospitalized, suggesting that most were mildly infected.

These subjects underwent magnetic resonance imaging of the brain before and after infection.

The researchers analyzed the structural changes in their brains and found three major ones.

First, COVID-infected participants had a significant reduction in brain volume, commonly known as brain atrophy, suggesting a possible increase in the incidence of dementia. Compared to the control group, the average extra loss of brain volume was 0.2 percent to 2 percent in the COVID-infected patients.

Second, the areas of the brain with reduced volume are mainly the orbitofrontal cortex (associated with decision-making processes), and the gray matter thickness of the parahippocampal gyrus (associated with cognition, emotion,

and memory). Here, volume was lost to a greater extent, suggesting an increased risk of brain fog.

Third, the damage to areas associated with the olfactory cortex was also significant.

More importantly, this suggests that the SARS-CoV-2 virus's damage to the brain isn't related to the severity of the disease. Structural and functional abnormalities of the brain can occur even in mild cases.

As aforementioned, Omicron infection doesn't have a high rate of severe disease or mortality, which means that there are a lot of mild cases. However, it can also cause long COVID, the sequelae of the COVID-19 infection, including dementia and neurological diseases, as mentioned in the earlier study.

Of course, studies have reported that the rate of long COVID due to Omicron infection is half of that by Delta. However, because of the large increase of the infected population, the number of long COVID patients due to Omicron isn't necessarily less than that of the previous variants.

The Brain Has the Ability to Regenerate: Long COVID Can Be Reversed

There's at least one cause for every disease, and it may be complicated. If the underlying causes can be found and resolved, then the disease may be cured or even reversed.

What's behind the neurological damage caused by the COVID-19 infection?

I have been following the neurological and psychological topic of COVID-19 for a long time, and I have read a lot of research. I also have previous research experience in neurology. According to my understanding and conclusion, although the SARS-CoV-2 virus strikes the human nervous system on seven aspects, the most severe cause lies in the virus's lethal strike of the neural stem cells.

In other words, the attack of the SARS-CoV-2 virus on neural stem cells leads to the destruction of the mechanism of neural cell regeneration in the brain, which is the crux of the problem.

Even if there appears to be severe damage to the brain, there are still ways to repair it. Scientists have discovered that the human brain has the ability to repair and regenerate itself.

The brain's regeneration ability was previously thought to be impossible, and this was a conclusion once written in textbooks. Since 1960, scientists have presented convincing evidence that brain nerve cells in adult animals or adult humans can regenerate.

For instance, scientists have found that the hippocampal region produces 600 to 700 new neurons per day. Of course, the brain has a total of 100 billion cells, and these 600 to 700 cells may not seem to be a lot. However, it shows that the brain is capable of regeneration, which is a key mechanism for maintaining brain plasticity and resilience.

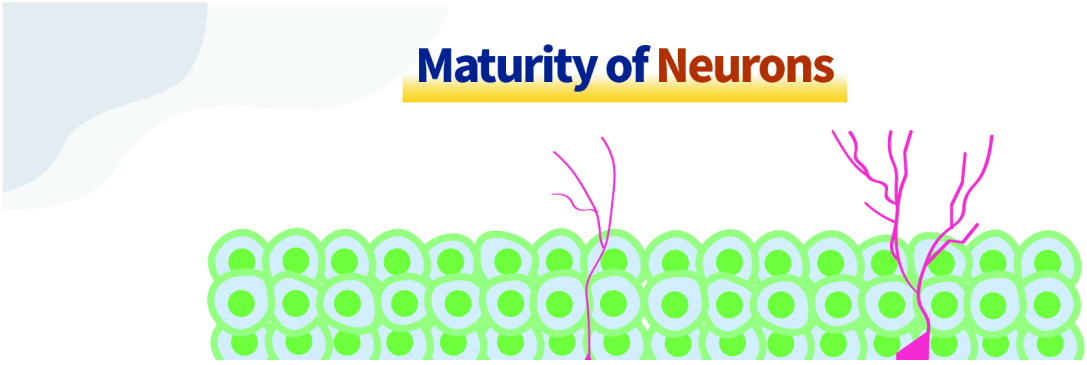
And it's this mechanism that the SARS-CoV-2 virus attacks, and it's this regenerative power that it inhibits. So to solve the problem of neurological sequelae after the COVID-19 infection, we have to study it from the perspective of regeneration.

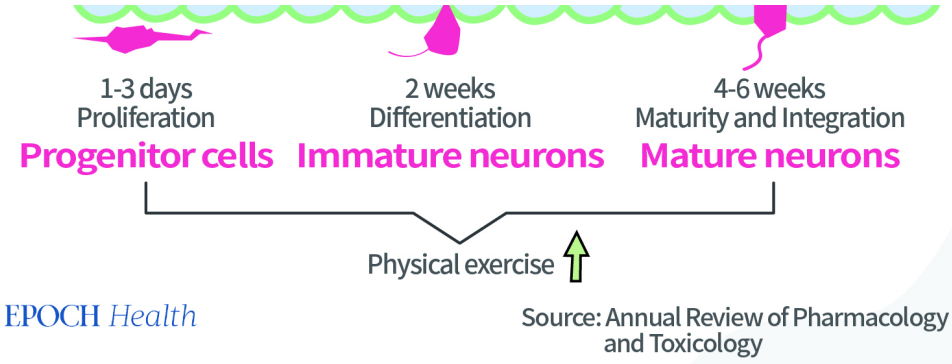
The main areas of nerve cell regeneration are the subventricular zone/olfactory bulb (as they are linked together), and parahippocampal gyrus.

The SARS-CoV-2 virus attacks the olfactory bulb and parahippocampal gyrus.

These two areas are like nerve cell manufacturing plants in our body and are the most important locations for nerve cell regeneration. In other words, the SARS-CoV-2 virus attacks the core of the brain—the area responsible for nerve cell regeneration. This is why the sequelae of nerve damage caused by the COVID-19 infection last so long and are so far-reaching.

So how long does the nerve cell regeneration process take?





One would certainly hope that this process is as fast as possible. In fact, nerve cell regeneration isn't slow. It takes three days for neural stem cells to generate neural progenitor cells, another two weeks to differentiate into naïve nerve cells (i.e., immature neurons), and another four weeks to develop into mature nerve cells. So the entire process usually takes at least six to seven weeks.

Ultra-Simple Aerobic Exercise for Nerve Cell Regeneration

Nowadays, nerve cell regeneration is a popular research topic. Many scientists are using methods such as neural stem cell implantation and neurotrophic factors; however, there are significant limitations in terms of applicability and effects.

I've consulted a lot of literature to find methods that are convenient, accessible, and also effective in helping the mind and body. There are, indeed, many more natural methods, and I can introduce them later when I have the opportunity.

Here, I'm presenting to you one of the simplest, cost-free, easy-to-do ways to regenerate neurons that are readily available to everyone. This method is consistent, regular, relaxing, and voluntary aerobic exercise.

It's generally known that exercise can bring more blood flow to the heart, lungs, and even the brain. However, many people don't know that regular aerobic exercise can also promote the regeneration of brain nerve cells in adults.

Let's first take a look at the data from an animal experiment.

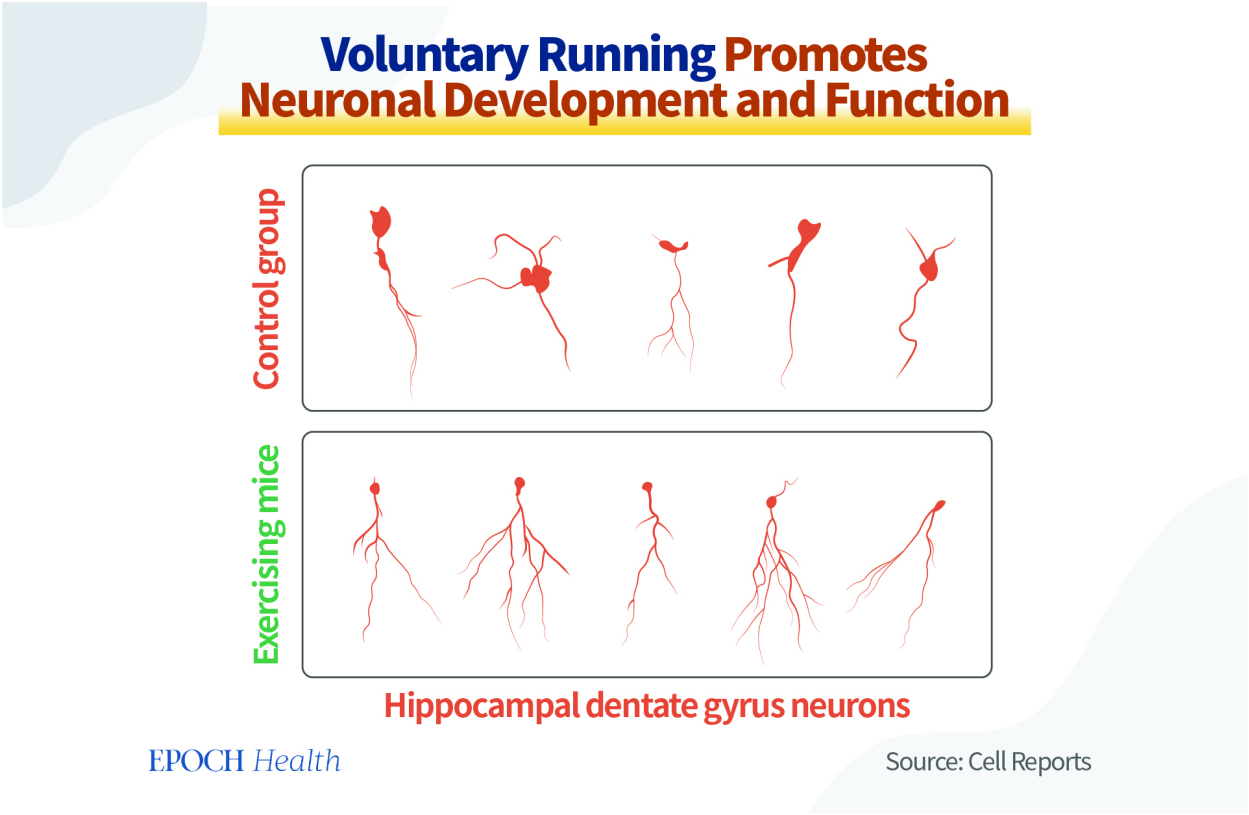
In a study at the Salk Institute for Biological Sciences in California, the researchers divided adult mice into two groups. The experimental group had running wheels and other favorable exercise conditions in their cages, while the control group didn't. It was found that after four weeks of voluntary and relaxing exercise by the adult mice, the regeneration of their hippocampal dentate gyrus

nerve cells was significantly increased.

The mice in the experimental group had regenerated approximately three to four times more nerve cells than those in the control group.

Moreover, the exercise accelerated the development of their regenerative neurons.

In 2017, some Argentinian neuroscientists published a study in Cell Reports. The experimental design was similar to that of the previous study. This study discovered that after 21 days of exercise, the newly grown neurons of the exercising mice were significantly more mature, with dendrites four times longer and more branched out than those of the sedentary (with no running exercise conditions) mice.



The neurons of sedentary mice in the graph resembled small bean sprouts, while those of exercising mice resembled well-grown bean sprouts.

According to the results of an electrophysiological function test, the granule cells of sedentary mice lacked action potentials or function. The granule cells of the exercising mice were repetitively discharging electricity, indicating that they were transmitting information and communicating with other neurons.

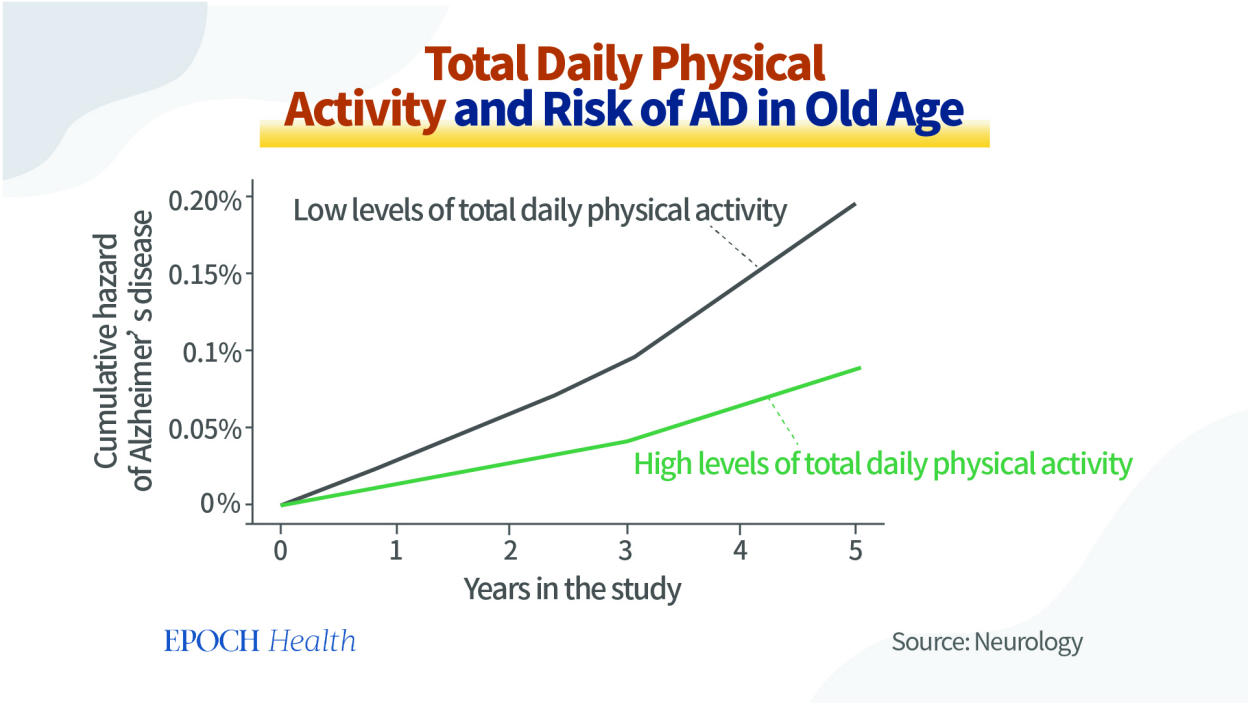
The development of nerve cells is only accelerated after a long period (three weeks), instead of a short period (one week) of exercise. At one week, the nerve cells haven't yet undergone so many structural and functional changes.

So, does effective exercise have to be running?

Not necessarily. Walking, daily grocery shopping, and household chores, which are related to physical activities, are all effective exercises.

How much physical activity should we undertake every day in favor of neuroregeneration? There are two studies that can give us some insights.

The first is a prospective observational cohort study in which 716 older adults without dementia were continuously observed for their daily physical activity over four years.



After four years, 71 subjects developed clinical Alzheimer's disease, which is a form of dementia, while those with high levels of total daily physical activity had about a 53 percent lower risk of Alzheimer's disease.

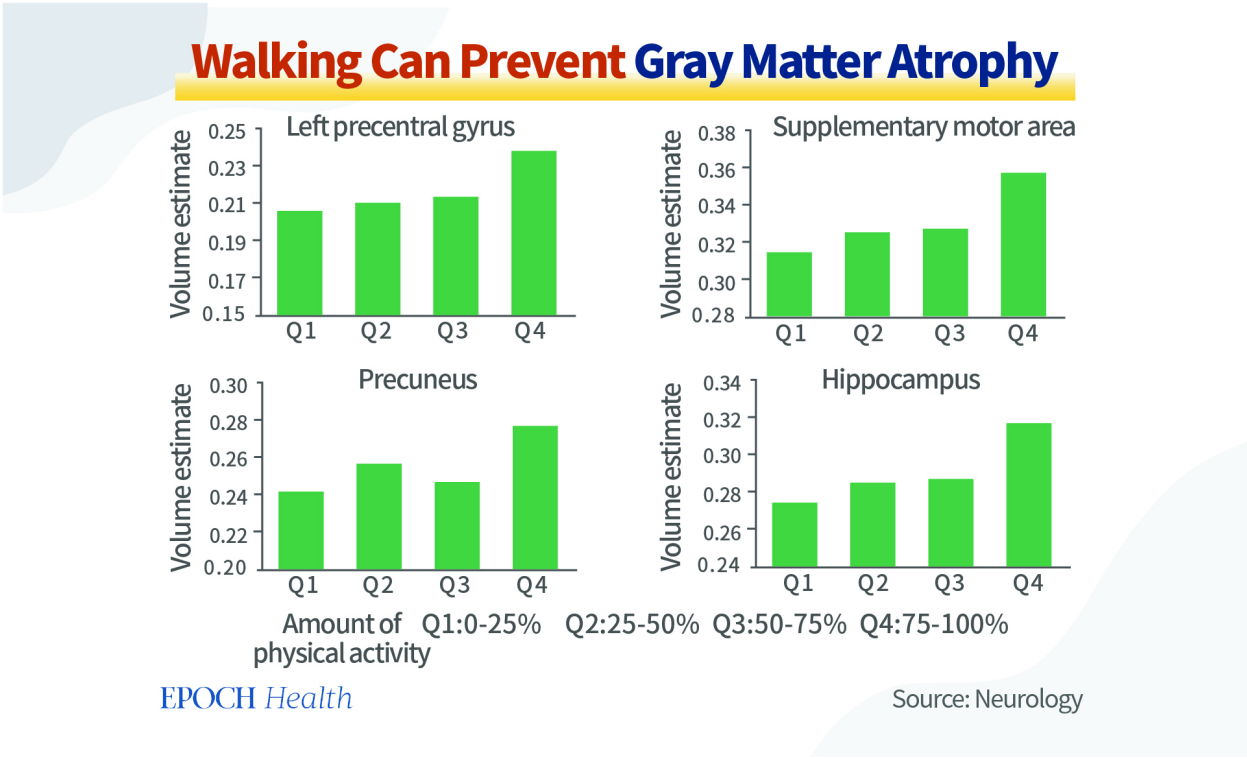
The design of this study was rigorous, and the analysis excluded other confounding factors that might influence the onset of dementia in old age, including age, gender, education, social and cognitive activity, as well as factors such as current level of motor function, depressive symptoms, chronic health

conditions, and APOE gene allele status.

That is, these confounding factors were balanced in both groups of older adults. The study concluded that daily physical activity level was an independent predictor of the onset of dementia in the elderly.

In another study, which was more detailed, 299 adults (with a mean age of 78 years) were followed up to examine the association between gray matter volume, physical activity, and cognitive impairment.

In this study, physical activity was calculated as the number of blocks walked in a week, and gray matter volume was an index associated with brain regeneration.



Based on their amount of physical activity, the investigators divided the 299 subjects into four groups from Q1 to Q4 (Q1 group had the lowest activity, and Q4 group had the highest activity). After observing them for 13 years, it was discovered that the gray matter volume in the Q4 group was significantly larger than those of the other three groups with less amount of physical activity. This difference was statistically significant, while there was no difference in the gray matter volumes of the other three groups.

Furthermore, the Q4 group had a twofold lower risk of cognitive impairment than the other groups after 13 years.

So, how much did the Q4 group walk each week?

They walked a cumulative total of 72 blocks per week (around six to nine miles per week).

Therefore, we can tailor the amount of workout and exercise to our own conditions.

So, reflecting on the fact that during the COVID-19 pandemic, lockdowns have been imposed across the globe, and some people couldn't go out and exercise freely, it wasn't beneficial to the neuroregeneration of their brain.

The Body Needs an Organic Balance of Movement and Stillness

Some health signals are simple yet easily overlooked. In fact, the human body and mind are closely related.

In addition to the need for nutrients such as glucose and oxygen, the brain's self-repairing and regenerative functions are facilitated by daily soothing, relaxing, and voluntary exercise.

We have previously mentioned the benefits that sitting in meditation brings to the brain. This isn't necessarily conflicting with the exercise advice. The human body is one organic equilibrium that requires a balance of movement and stillness. If our movement and stillness can be dynamically balanced well, our brains benefit from such dynamic equilibrium quite a lot.

This is why we have always emphasized that aerobic exercise that makes you feel comfortable is the best. We can all arrange it appropriately according to our life and work schedule.

There's a saying: "Walking a hundred steps after each meal can help you live to be 99 years old." Such exercise is not only helpful to our intestines and digestion, but also beneficial to our brain and nerve regeneration. It's easy, cost-free, and natural. It could potentially help us to prevent premature aging and the neurological/psychological sequelae of COVID. Here, you can see again another example of how one small, healthy habit could make us healthier and even change our lives.

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Dr. Yuhong Dong

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Mercura Wang

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Mercura Wang is a health reporter for The Epoch Times. Have a tip? Email her at: mercura.w@epochtimes.nyc