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Zhiyuan-Cardiac conductive disease

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Edith/Katherine/Rachel--Mitochondria DNA

Cheryl Icey-current situation and future development of AIHA treatment

polaris-Gut-Brain Axis and Mental illness

Wakanda neuroscience and psychoanalysis

Charlene liver cirrhosis

Tina&Marina Stratospheric Aerosol injection

1

ENGLISH VERSION

Chinese version is in the back

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Vocabulary

Intravenous: taking place into veins
Antioxidant: a substance that slows down the rate at something decays because of oxidization
Oxidative: a chemical reaction that takes place when a substance comes into contact with oxygen or another oxidizing substance.

Radicava ORS for patients with ALS

Situation

Amyotrophic lateral sclerosis (ALS), also known as Lou Gehrig's disease, is a progressive and fatal neurodegenerative disease. There is currently no cure for ALS. In May 2022, the United States Food and Drug Administration (FDA) approved a new drug application, which includes Mitsubishi Tanabe Pharma America Inc.'s RadicavaORS (edaravone), an oral suspension used to treat ALS. Edaravone is a free radical scavenger believed to alleviate the effects of oxidative stress, which may be a key factor in the onset and progression of ALS. Currently, the drug can only delay the progression of the disease and there is no known cure for ALS.

Know more about ALS

When we talk about the "Ice Bucket Challenge" that was popular worldwide a few years ago, we may think of a rare disease - amyotrophic lateral sclerosis (ALS), also known as Lou Gehrig's disease. ALS is a progressive and fatal neurodegenerative disease that cannot be cured. Famous British physicist Stephen Hawking was one of the rare cases of ALS, having survived 55 years with the disease, while most ALS patients have a life expectancy of approximately three to five years.

This disease affects certain motor neurons in the brain and spinal cord, causing them to die. Motor neurons transmit information from the brain to muscles, and when these neurons die, the information cannot reach the muscles, causing muscle weakness, wasting, and eventually loss of voluntary movement. As the disease progresses, patients gradually lose their ability to move and even swallow, and eventually suffer from respiratory failure and death. The whole process is like being "frozen", as patients watch their physical abilities gradually deteriorate in their conscious state.

The exact cause of ALS is unknown, and anyone can develop the disease. It may be caused by genetic defects, hereditary factors, or exposure to environmental toxins, among other issues. However, ALS can generally be divided into two types: familial and sporadic. Familial ALS is when a family member has ALS, but it only accounts for 10%, while sporadic ALS is when there is no family history of the disease.

Igniting hope for those with ALS - research on new drugs

What is Edaravone?

Due to the elusive and uncertain nature of ALS, there is still no medication that can effectively treat the disease, but there are two drugs, Riluzone and Edaravone, that can effectively improve the patient's survival state and slow the progression of the disease. Edaravone is a kind of brain protector (free radical scavenger), which can not only treat ALS, but also treat ischemic stroke. Its mechanism of action is to relieve oxidative stress by free radicals, prevent oxidative damage to brain cells, and protect the nervous system with its antioxidant ability, thereby slowing the progression of ALS.

Clinical Trial

In a key phase III clinical trial, conducted as a double-blind placebo-controlled study with 137 ALS patients, Radicava's impact on ALS was evaluated throughout the trial using the revised ALS Functional Rating Scale (ALSFRS-R). The results showed that after 24 weeks of treatment with Radicava, patients had a 33% reduction in functional disability, which was significantly better than the placebo. In another global phase III clinical trial lasting 24 weeks, the safety and tolerability of Radicava ORS oral suspension were evaluated in 185 ALS patients. 5% of patients experienced adverse reactions, including muscle weakness, falls, fatigue, headaches, and other problems.

Conclusion

Compared to intravenous injection, Radicava ORS as an oral medication is more convenient. Although there is no drug available that can completely cure ALS, Radicava ORS can improve patients' quality of life and slow the progression of the disease. To date, scientists still do not fully understand the causes of ALS, and the disease can occur in anyone. Therefore, our best preventive measures are early detection, early diagnosis, and early treatment.

About Radicava ORS

Radicava ORS is an oral suspension developed by Mitsubishi Tanabe Pharma for the treatment of ALS. Its US subsidiary, Mitsubishi Tanabe Pharma America (MTPA), received FDA approval for the new drug application in May 2022. Edaravone products can be divided into intravenous injection and oral suspension, and Radicava ORS belongs to the latter. The components and mechanisms of intravenous injection and oral suspension are the same. Oral medication provides greater convenience for patients, and the 5ml portable pack of Radicava ORS allows patients to take the medicine home without the need for reconstitution and refrigeration. The drug is very flexible and convenient, with the only caveat being that it needs to be taken on an empty stomach in the morning.

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SMART

vol. 2

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#1 THE DARK MATTER

According to the Centers for Disease Control and Prevention, CDC, Alzheimer's disease also known as Senile dementia is an irreversible, progressive brain disease that begins with mild memory loss and eventually leads to the inability to talk and respond to the surrounding environments. Throughout the world, it is the most commonly diagnosed form of dementia. The Alzheimer's Association provides further information in its article "Alzheimer's Disease Facts and Figures" in which it is estimated that more than 55 million people worldwide suffer from Alzheimer's disease, and one person develops dementia every three seconds.

Even more, research indicates a decreased aging for Alzheimer's disease diagnosis. Recently, the Journal of Alzheimer's Disease, a well-known journal in China, claiming to have found a 19-year-old teenage male have been diagnosed with Alzheimer's disease. The paper came out like a stone cast into a lake stirring up a thousand waves online. "Youth dementia" has entered the social discussion due to the increasing prevalence of young people forgetting things.

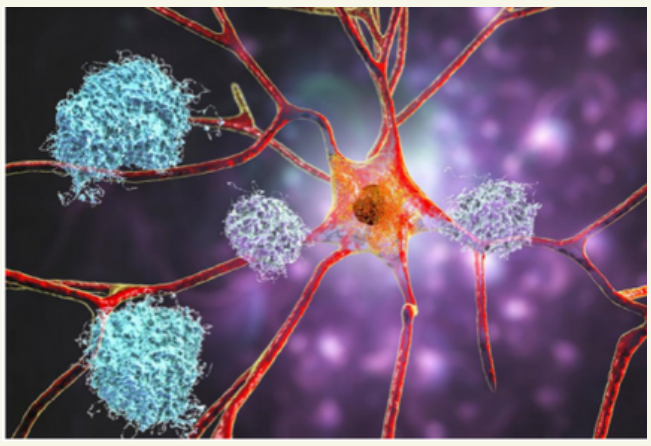
We now understand how important it is, so let's take a look at some scientific information we should be aware of. Alzheimer's disease affects the brain in complex ways that require years of professional study, but reading this article gives you a good idea of how it works. Changes in the brain often begin before symptoms appear. It is possible to see detrimental changes in the brain already at this very early stage of Alzheimer's disease. Beta-amyloid plaques and tau tangles are building up in the brain, neuronal connections are disrupted, and neutrons lose their functionality. As neurons die, other parts of the brain shrink and become affected, causing Alzheimer's to become terminal. This damage appears to occur first in the hippocampus and entorhinal cortex, which are the parts of the brain responsible for memory. When Alzheimer's disease reaches its final stages, the damage has spread and brain tissue shrinks considerably. As the patient's body stops functioning, the patient may be bedridden most of the time or even all day, leading to death.

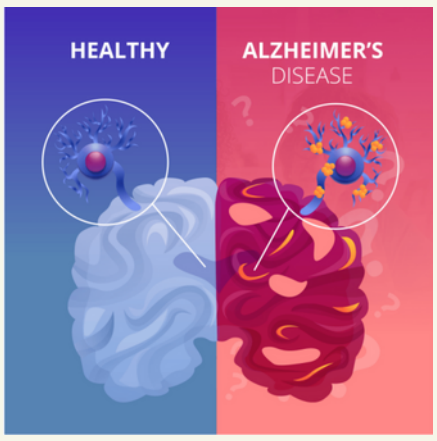
WORD BANK

Alzheimer's Disease: A progressive mental disorder that disrupts memory and other essential functions.

Beta-amyloid: The amyloid beta peptide is a 36-43 amino acid peptide that is largely responsible for the plaques found in the brains of Alzheimer's patients.

Mild cognitive impairment (MCI): It is a phase between the expected decline in memory and thinking caused by aging and the more sever decline caused by dementia.





#2 HOW IS ALZHEIMER'S DISEASE TREATED?

There is no existing medication that alters the underlying disease process in Alzheimer's disease because human brains are complex. Currently, treatment focuses on maintaining the mental function, treating the inflammation underpinning the disease, and managing behavioral symptoms.

Several possible interventions are being developed and tested in multiple clinics. As part of the research, therapies are being evaluated as well as non-drug approaches including physical activity, diet, cognitive training, and combinations thereof.

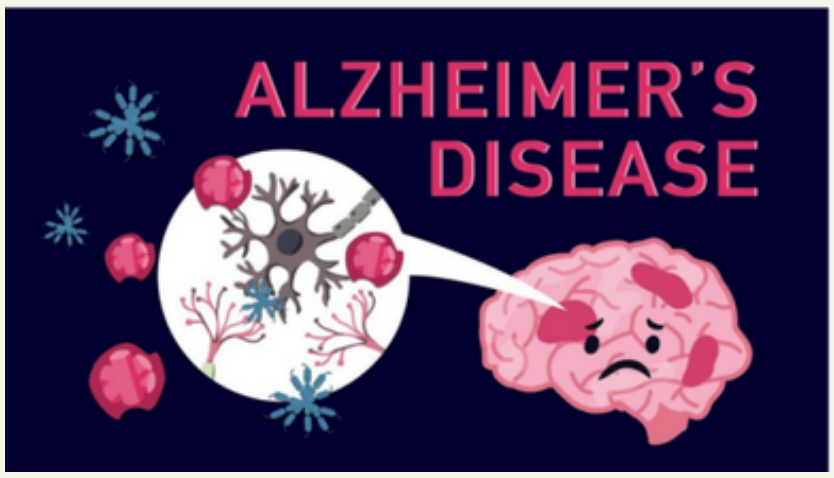
#3

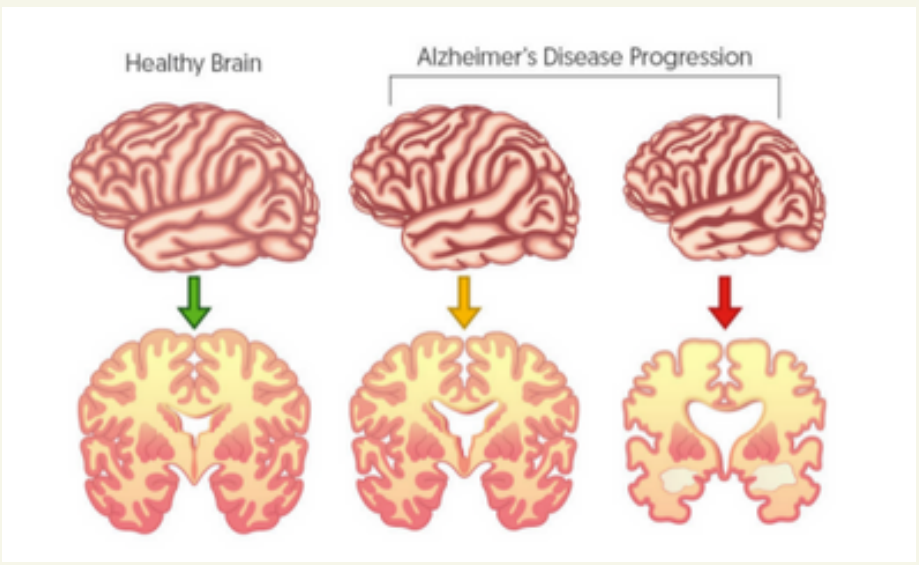
MEDICINE BREAKTHROUGH

Although, some of the medications can help reduce symptoms and alleviate certain behavioral problems. However, these drugs do not alter the underlying disease process. They work for some, but not all, people and may only be effective for at limited time. And Aducanumab (Aduhelm TM) plays an important role when it comes to this situation.

Aducanumab was approved by the U.S. Food and Drug Administration (FDA) using the accelerated approval pathway. This process aims to approve drugs for a serious or life-threatening condition that offers a meaningful therapeutic regimens advantage over current treatments (i.e BioNTech, Pfizer vaccine). It was also the first therapy shown to effectively slow the progression of Alzheimer's disease by removing the beta-amyloid plaques from the patients' brains, reducing the cognitive and functional decline in patients with early Alzheimer's disease.

Aducanumab takes effect by targeting and removing specific forms of beta-amyloid that accumulate into plaques, thereby decreasing the possibility of cell death and loss of the brain tissues in the memory area. Although the brain will continue making beta-amyloid, Aducanumab reduces the amount simultaneously.





#4

Prevention Tips:

Research suggests that a variety of factors other than genetics play a role in the onset and course of Alzheimer's disease. Ongoing research will help us understand if and how making some changes in your daily life can reduce the risk of developing Alzheimer's disease. Here are some tips you and your family members can practice to prevent Alzheimer's disease.

1. Eat a balanced diet

To prevent Alzheimer's disease, it is important to eat a balanced diet and control the intake of salt and animal fats. Salt intake should not exceed 10 grams a day, and animal fats and sugar should be kept to a minimum.

2. Moderate Exercise

Consistent exercise can also prevent Alzheimer's disease. Exercise can improve our immune system. Movement of the hands is also critical. You can do easy finger dance to help energize the brain.

3. Find medical consultation

If the cause of the disease is clear, you should see a physician as soon as possible to avoid further harms.

#5

Although growing old and developing Alzheimer's disease do not equate, growing old is often not just about one person, but is closely related to the whole family.
Aging is not just a test of self-awareness and how to plan our lives, but also a serious test for the family.
This requires us to prepare for it as early as possible and to look at it from the perspective of both the individual and the family.
We hope that we can pay more attention to the physical and mental state of our parents and put their aging into our life planning. Along with paying attention to the details of life, it is also important to take your loved ones for regular medical checkups.

SMART

vol. 2 *author: Sindy*

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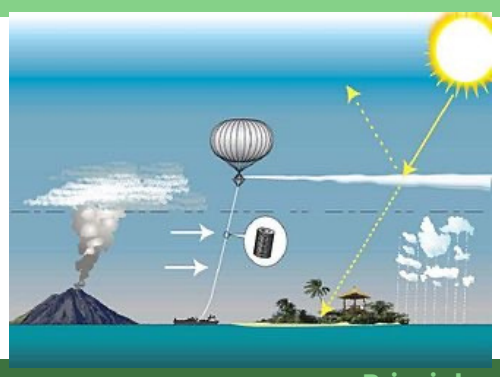
Stratospheric Aerosol Injection: A Promising Solution for Environmental Protection

Introduction

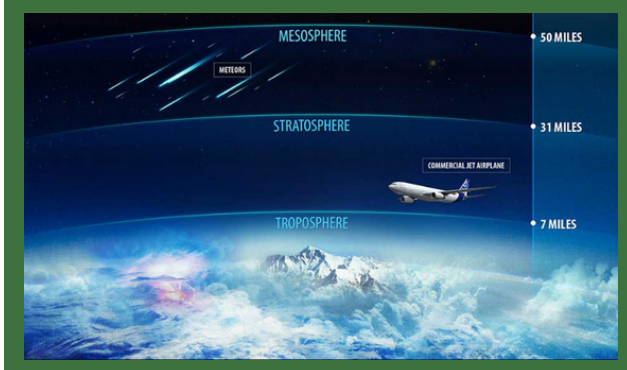
Environmental protection is currently one of the most pressing issues. As the earth is facing unprecedented environmental challenges such as global warming, climate change, and ozone depletion, it is becoming increasingly important to explore and implement innovative solutions to safeguard the environment. Stratospheric Aerosol Injection (SAI) is one such promising solution that has been gaining attention in recent years. It aims to reduce the amount of solar radiation reaching the Earth's surface. In this essay, we will explore what SAI is and how it works to protect the environment as well as examine its overall impacts on the environment.



Key Words

Global warming
Solar geoengineering
Stratospheric Aerosol Injection
Aerosols

Principle

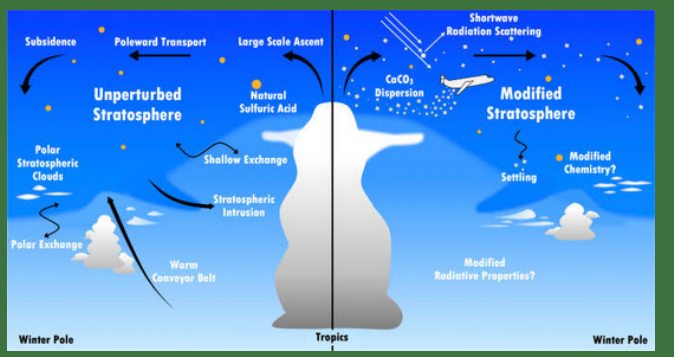


The primary role of SAI is to reflect sunlight and maintain the Earth's energy budget.

Firstly, atmospheric aerosols cool the Earth. SAIs do this by interacting with sunlight entering the atmosphere; when scattering sunlight back into space, the aerosols cool the Earth, while when absorbing sunlight, the area near them warms, but the atmosphere below them cools. It involves increasing the albedo of the Earth by injecting small reflective particles into the stratosphere. This increase in albedo is not achieved by injecting aerosols themselves into the stratosphere, but usually by injecting chemical precursors such as sulphur dioxide ($SO2$), which are then converted into aerosols by physical and chemical processes.

Primary aerosol formation, also known as homogeneous aerosol formation, occurs when gaseous $SO2$ combines with oxygen and water to form an aqueous sulphuric acid solution ($H2SO4$). This acidic liquid solution takes the form of a vapour and condenses on particles of solid material, which may come from meteorites or from dust carried from the surface to the stratosphere. When $H2SO4$ vapour condenses onto existing aerosol particles, secondary or heterogeneous aerosols are formed.

Models and theories suggest that increasing the amount of aerosols in the atmosphere will cool the Earth and thus mitigate some of the effects of greenhouse gases on our planet.



What is SAI?

SAI is a geoengineering technique that involves injecting tiny reflective particles into the atmosphere, specifically the stratosphere, to reflect sunlight back into space and cool the Earth's surface. The idea was developed out of observations and first proposed in 1974 by the Russian climatologist Mikhail Ivanovich Budyko. This technique mimics the cooling effect of each volcanic eruption, which injects large amounts of sulfur dioxide, hydrogen sulfide, finely powdered salt or calcium carbonate into the atmosphere and causes 1 to 2 years of cooling over large areas of the planet.

How Does SAI Work?

SAI involves spraying tiny reflective particles or aerosols to reflect sunlight into the stratosphere in order to cool the planet via global dimming and increased albedo. The delivery system can include tethered balloons, high-altitude airplanes or even artillery.

Advantages

Firstly, stratospheric aerosol injection is feasible with current technology and its advantages outweigh its disadvantages.
It is considered to be relatively safe for the environment. Because volcanoes consistently inject sulphate aerosols into the stratosphere, the biosphere naturally processes sulphate in a variety of ways in the sulphur biogeochemical cycle. In addition to sulphate, other reflective aerosols have been considered for this method of solar radiation management. These aerosols include carbon black, aluminium metal, aluminium oxide and barium titanate.
It can also be implemented in a very short period of time and at a relatively low cost. As stratospheric aerosols naturally fall out of the atmosphere, the benefits/effects of this method are temporary and usually last 1 to 2 years.

drawback

Unfortunately, there are dangers associated with stratospheric aerosol injection. This method may reduce the amount of rainfall in some parts of the world. Reduced rainfall leads to reduced crop yields and interruptions in freshwater supplies, which can lead to hunger and misery. If this approach is used, it is important to develop and implement measures to protect people and save lives and livelihoods.

They also include geopolitical, security, socio-economic and moral risks. Large-scale implementation of stratospheric aerosol injection (SAI) could lead to catastrophic transboundary damage. It is crucial to address the issue of compensation for potential victims of such damage before implementation of the technology begins. However, existing international liability rules are unable to provide fair and effective compensation for SAI damage and international law has so far not provided for a specific liability regime for SAI.

Conclusion

In conclusion, SAI is a promising solution for environmental protection, as it can effectively and cheaply mitigate the impacts of global warming, reduce harmful UV radiation, and restore the Earth's ozone layer. However, SAI is also facing challenges and uncertainties that need to be addressed, for example, the long-term effects of SAI on the environment and climate are not well understood, thus more research is necessary to evaluate its potential risks and benefits. As such, SAI should be considered together with the many other potential solutions including renewable energy development, energy efficiency improvement, carbon capture and storage, etc. Only the cooperation of different approaches can maximise their overall effects on environmental protection.

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Exercise Can Lead to Epigenetic Changes

Ray & Olivia

Abstract: Six weeks of physical exercise leads to epigenetic changes in the skeletal muscle cells of young men, occurring in regions of the genome associated with disease. Scientists report that their study suggests, for the first time, how exercise reshapes DNA in the skeletal muscle to establish new signals for maintaining bodily health. DNA is the molecular guidebook present in all of our cells. Some parts of our DNA are genes, instructions for building proteins (building blocks of the body), while other parts are called enhancers, which regulate which genes turn on or off and in which tissue. For the first time, scientists have discovered that exercise alters enhancers in known disease risk-associated regions of our DNA.

Keywords:
chronic disease; diabetes; cholesterol; susceptibility; adrenaline; GWAS; histone; skeletal muscle.

I. Experimental section:

Genes in the human body are instructions for building proteins, while other special parts called enhancers regulate when genes are expressed. Scientists have for the first time discovered that exercise alters enhancers in relevant regions by regulating the methylation level of our DNA. Gene methylation refers to the selective addition of a methyl group to cytosine (C) in CpG dinucleotides of DNA molecules to form 5'-methylcytosine under the action of enzymes. CpG dinucleotides are often located near gene transcription regulatory regions. Methylation can cause changes in chromatin structure, DNA conformation, DNA stability, and hence regulate gene transcription and expression.

Scientists recruited healthy 25-year-old participants and had them participate in a six-week endurance exercise program. They collected live muscle tissue slices from their thighs before and after training, and examined whether their DNA epigenetic characteristics changed after training. Scientists found that many enhancer structures in the skeletal muscles of young people underwent changes after completing the training. By linking enhancers with information in genetic databases, they discovered that many regulated enhancers have been identified as hotspots of individual genetic variations.

Scientists speculated that exercise has a benign effect on certain organs far from the muscles, such as the brain, which may be achieved through fluid regulation. At the same time, performing certain exercises can reshape enhancers in skeletal muscles, especially those associated with cognitive abilities. This provides scientists with a new direction for studying the induction of muscle-secreted factors in the brain through exercise training.

The results showed that the demethylation status of the PGC-1α, PPAR-δ, and PDK4 genes depends on the intensity of exercise. The study found that the higher the intensity of exercise, the higher the demethylation level observed in muscle biopsies.

When the methylation level of the promoter region is high, the likelihood of binding with transcription factors is relatively low. Transcription factors are proteins that can control gene expression. This means that methylation will regulate gene expression. The experimental results showed that the expression of PGC-1α, PPAR-δ, and PDK4, which are genes related to energy metabolism, increased after exercise.

In addition, demethylation can also occur when muscle cells are exposed to excessive caffeine during cultivation. This is because caffeine can promote the release of calcium from the sarcoplasmic reticulum, which can cause simulated muscle contractions to some extent. Therefore, calcium may activate demethylation.

II. Gene

A gene is a sequence of nucleotides that is necessary to produce a polypeptide chain or functional RNA. The interdependence between environment and genetics governs important physiological processes such as reproduction, cell division, and protein synthesis in life. All life phenomena such as growth, decay, disease, aging, and death are related to genes. Genes exist in the nucleus of each cell and contain information for bodily growth and development. Genes control the appearance and function of the body and determine your height. DNA is the genetic blueprint that contains instructions for organisms to manufacture proteins. Proteins are essential for all life forms, as they are a component of most biological molecules.

III. Benefits of Physical Exercise:

1.Physical exercise can improve physical fitness and increase resistance.

Long-term exercise can enhance cardiopulmonary function, improve blood circulation, keep the body's energy and blood circulation in good condition, accelerate the excretion of waste, and promote metabolism. Exercise can promote protein synthesis, enhance muscle elasticity, increase skeletal muscle density, increase joint stability and flexibility, and reduce the risk of disease. The most frequent exercise can reduce the mortality rate of cancer by 70% for non-smokers. Even frequent exercise smokers can reduce the mortality rate of cancer by 54%. It can also reduce the risk factors for cancer, hypertension, and hyperlipidemia by 50%.

Physical exercise can also increase the level of endorphins in the plasma of patients with mild cognitive impairment, improving their cognitive abilities and memory. Exercise can also reduce neural inflammation and alleviate symptoms in patients with brain damage. Scientific research has shown that exercises such as walking, running, playing musical instruments, typing, and picking beans can effectively stimulate regional cerebral blood flow, which helps to prevent and slow down dementia in the elderly. People who lead sedentary lifestyles are twice as likely to suffer from Alzheimer's disease as those who exercise regularly.

2.Physical exercise can regulate mood and uplift spirits.

Exercise doesn't produce happiness per se, but it does produce feelings of excitement and stimulation. Although the dopamine produced by exercise is different from the dopamine that brings us happiness and is produced in a different part of the brain, it does not mean that exercise cannot regulate our emotions. Endorphins are endogenous opioid neuropeptides that can bind with opioid receptors and produce a feeling of pleasure. When we exercise, our body continues to secrete endorphins, which can make us feel relaxed, happy, and relieve stress.

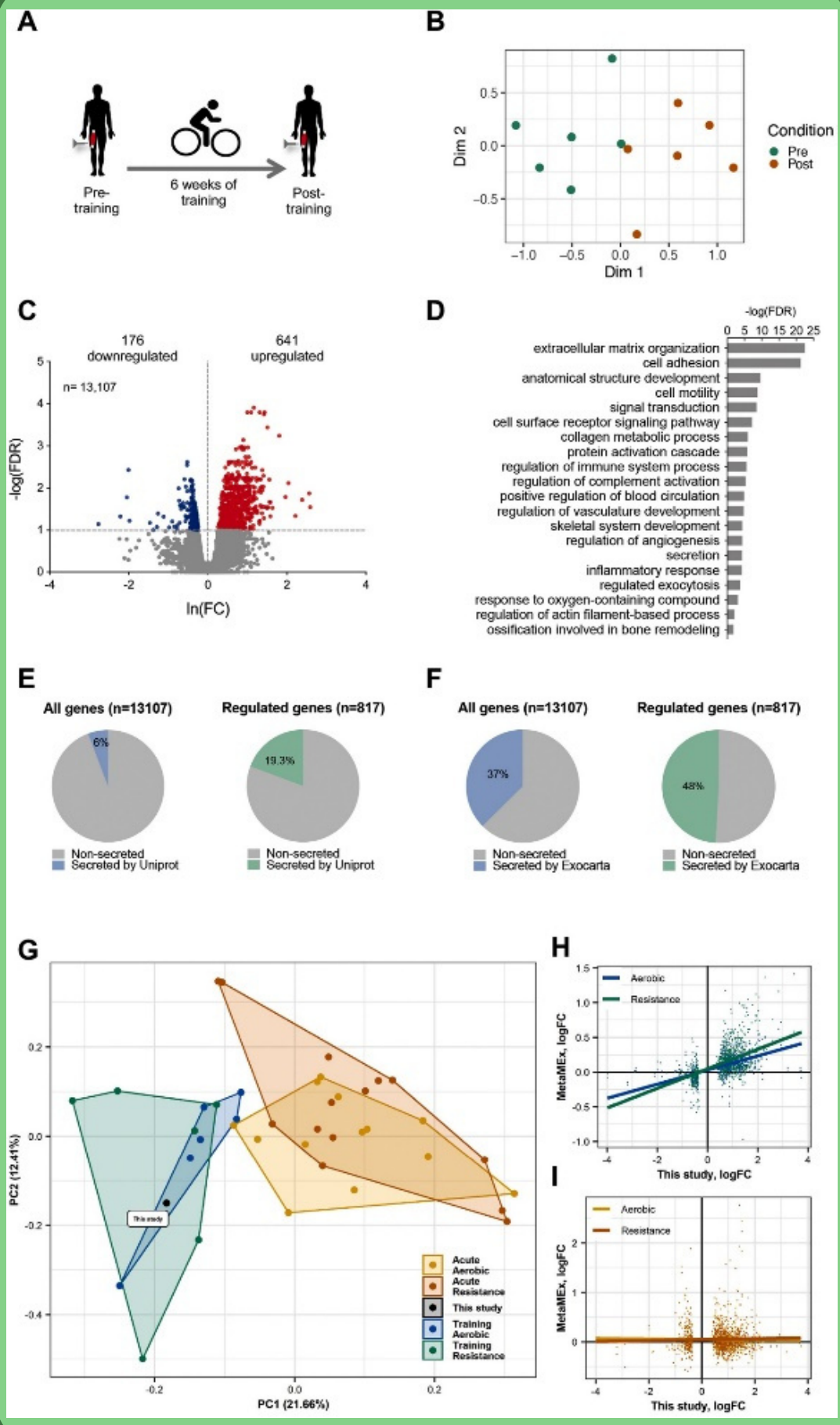
At a macro level, physical exercise uses physical activity as its basic means to enhance physical fitness, promote health, and cultivate various psychological qualities of people. With the development of the society and improvement of living standards, people's needs for psychological fulfillment are higher than their needs for material goods. People's understanding of sports is not only limited to the aspect of physical health, but also hoping to gain more spiritual enjoyment through participating in sports activities. It is not just about physical fitness, but more importantly, it provides people with a sense of release in terms of their spirit and nerve, pleasure, a sense of achievement, and emotional relaxation. These are all the spiritual values that sports bring to people. The higher the standard of living, the more people focus on the spiritual values of sports.

IV. How to Exercise Correctly

When it comes to aerobic exercise for weight loss and slimming, it is recommended to maintain a heart rate between 60%80%, just on the edge of the body's comfort zone, and exercise for half an hour a day to achieve excellent results.
Keep yourself in a slightly breathless state when doing aerobic exercise. For example, when running, maintain a fast enough speed until you are slightly out of breath, continue for 12 minutes, then switch to fast walking, adjust your breathing, and repeat.
For better results, it is best to combine complex sports, such as practicing yoga, dancing, gymnastics, tai chi, and so on after 10 minutes of aerobic warm-up. These complex activities can involve all neural cells in the brain.

V.Conclusion:

Although it has been found that exercise can change genes, there is still a lot of room for improvement. Exercise is essential for each and every one of us, and what we need to do is to maintain a healthy body and create a better world.



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GUT-BRAIN AXIS AND MENTAL ILLNESS

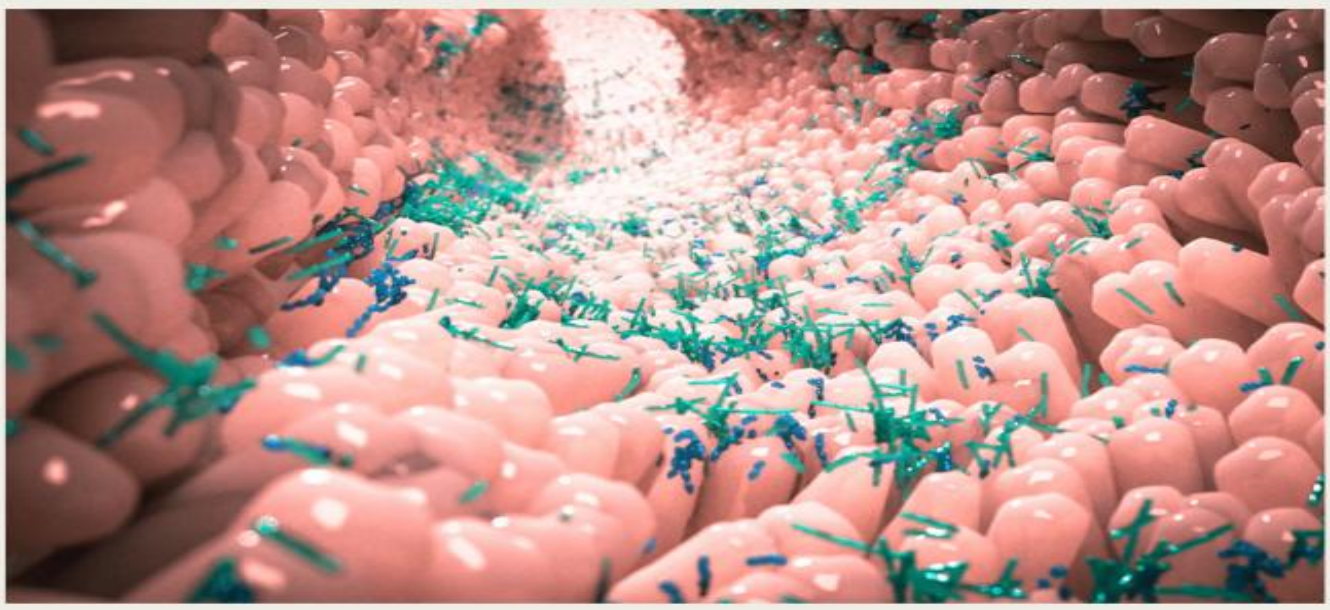
Keywords: gut microbiota; mental health; gut-brain axis

Abstract

In recent years, mental illness has garnered more attention due to the general increase in mortality rates. A wide variety of gastrointestinal symptoms, notably in the gut microbiota, which is characterized by certain changes, have been reported by a number of researchers to be present in individuals who suffer from neurological illnesses. This study investigates the connection between psychiatric disorders and the brain-gut axis and proposes a novel method to influence psychiatric disorders in a roundabout way by enhancing the gut microflora through the mechanism of their interaction. The method could have a positive impact on people's lives.

Introduction

In recent years, there has been a rise in the incidence of mental diseases, which poses a problem for an ever-increasing number of people and is reflected in the statistics pertaining to mental health. It is particularly prevalent among adolescents as a direct result of the effects of the environment (constant high levels of stress, depressing atmosphere and low levels of exercise, etc.). According to what has been seen in clinical patients, the etiology of the disease has a detrimental effect not only on the brain, but also on other physiological processes, most notably the digestive system. This is especially true for individuals who have been dealing with the ailment for a longer period of time. According to the findings of a number of research, persons who suffer from mental health issues experience gastrointestinal symptoms (constipation, vomiting,



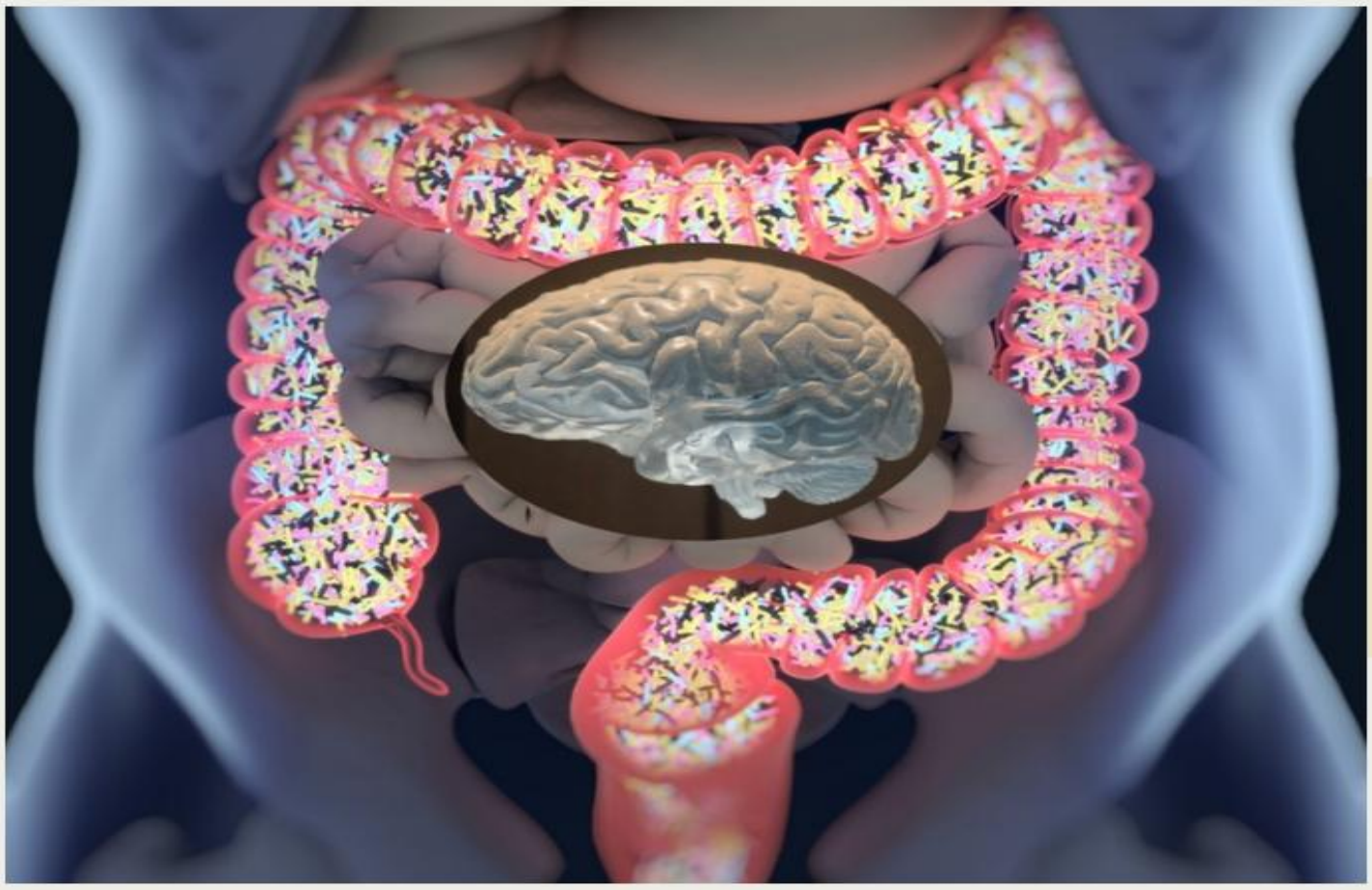
discomfort, abdominal pain, and flatulence) (Srikantha and Mohajeri). The digestive system and the brain are thought to be related, according to one popular hypothesis. Recently, a number of studies have proposed that the brain-gut axis can be utilized to examine the mechanisms that are behind the link between psychiatric diseases and the gut (Knuesel and Mohajeri). The investigation of the link between mental disease and the axis that links the brain and the gut may give us with a fresh perspective on how to approach the problem of resolving issues associated with mental health.

2. Discussion

2.1 Mechanisms linking mental illness and the brain-gut axis

The bacteria that live in a person's digestive tract have a significant impact on the individual's general state of health. There have been a lot of discoveries have been published in the scientific literature that provides the impression that different diseases may exhibit multiple variations of the same species of flora (Vijay and Valdes; Leung et al.). As a result, variations in the make-up of the microbiota in the gut can act as a predictor of gut health in an indirect manner. Alterations in the

microbiota of the gut have been linked to the development of neurological disorders (Butler et al.). According to earlier research (Megur et al.; Jiang et al.; Bostanciklioğlu), patients suffering from psychiatric disorders have ecological dysbiosis that is characterized by reduced diversity. There is a correlation between depression and significantly lower levels of bifidobacteria and lactobacilli (Aizawa et al.). It has been hypothesized that the deregulation of environmental systems may have a role in the development of neurological disorders (Tremlett et al.). Intestinal ecological dysregulation, which can lead to inflammation, may have its origin in increased intestinal permeability. There is a correlation between dietary inflammation and a higher susceptibility to acquire psychiatric diseases, which implies that the two go hand in hand



The greater propensity to acquire psychiatric disorders also has a correlation with dietary inflammation (Ratnayake et al.).The stimulation of inflammation has been linked by researchers to the early onset of psychological illnesses. This is a connection that was not previously known. It is extremely improbable that germs could have an are mediated by diet-induced alterations in the resident bacteria of the gut may contribute to the

the development of mood disorders that are reverse-promoted. There is a correlation between the production of dopamine and the reduction in the amount of biodiversity (Bharwani et al.). The production of serotonin can be significantly influenced when there is a reduction in the diversity and stability of the bacteria that live in the stomach (O'Mahony et al.). When it comes to the treatment of mental health illnesses, neurotransmitters including serotonin (5-HT), dopamine (DA), and norepinephrine are among the drugs that are prescribed the most frequently (NE). An imbalance in the bacteria that live in the gut causes a reduction in the production of neurotransmitters that are helpful for psychiatric rehabilitation and may have a negative impact on the evolution of the disorder. Hence, therapeutic techniques that target the dysbiosis of the gut microbiota in patients could be an effective strategy for preventing the progression of mental disease as well as improving the condition of mental illness.

Wang, Shugui, et al. "Targeting the Gut Microbiota to Influence Brain Development and Function in Early Life." 95 (2018): 191-201. Print.

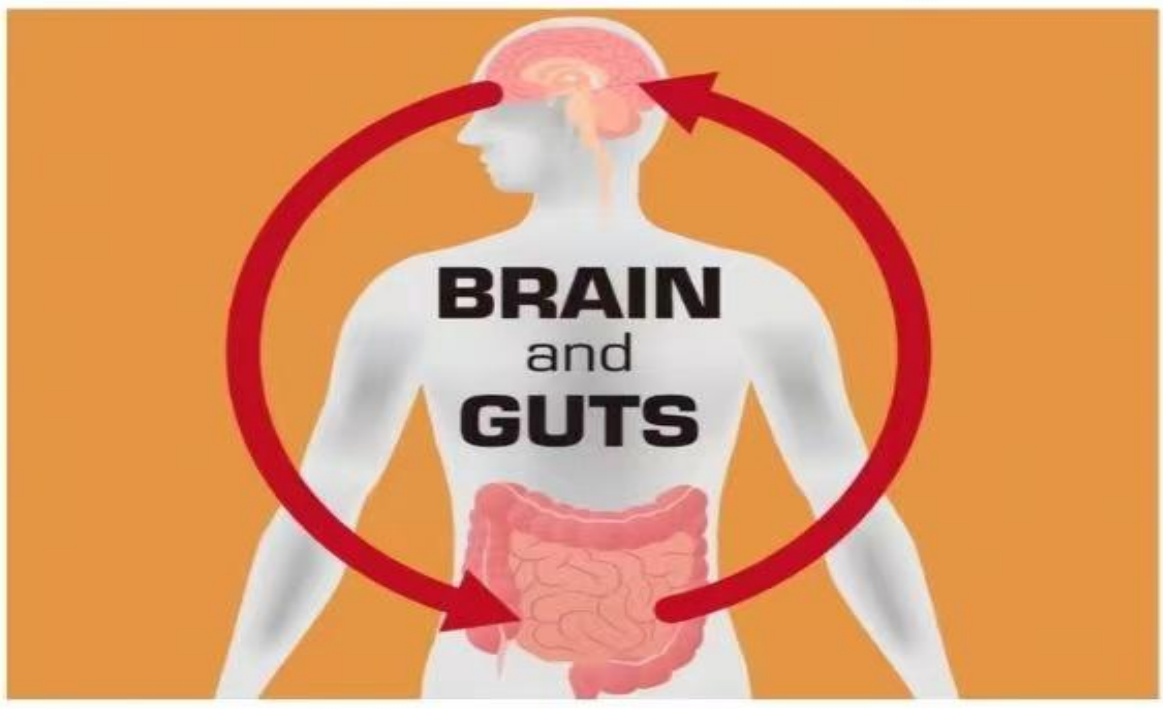
2.2 Using gut microbes to influence mental illness

Microbes that live in the intestines have been shown to have a major impact on a variety of neurological and behavioral conditions. Altering one's diet is an efficient way to bring about changes in the microbiota that live in one's digestive tract. Eating a diverse array of meals has the potential to have a discriminatory effect on the make-up of the microbiota. There is evidence to suggest that consuming an unhealthy diet can create ecological dysbiosis by lowering the amount of beneficial gut microorganisms. Those who suffer from mental illness are more likely to engage in activities associated with selective eating, which can result in nutritional inadequacies. According to the findings of studies, these behaviors have a significant bearing on the progression of mental illness (Kałużna-Czaplińska, Jóźwik-Pruska and Technology). At the same time, repairing ecological dysregulation may have a moderating influence on the psychological diseases that are connected with it. The management of microorganisms in the gut is tightly connected to the ideal ratio of beneficial bacteria to harmful bacteria that exists in the gut. Examples

GUT-BRAIN AXIS AND MENTAL ILLNESS

of common beneficial bacteria that are found in a digestive tract that is healthy include Lactobacillus, Bifidobacterium, and Lactobacillus rhamnosus. Probiotic therapy has been shown in a considerable number of clinical trials to give significant benefits to people who suffer from mental problems (Sanada et al.). Some strains of the bacteria Bifidobacterium and Lactobacillus have been proved to have beneficial impacts on the brain and behavior (Savignac et al.). Further research indicates that a combination of probiotics containing

Further research indicates that a combination of probiotics containing Lactobacillus and Bifidobacterium is advantageous for the enhancement of mood (Steenbergen et al.). According to the findings of recent studies, the beneficial probiotic bacterium known as Lactobacillus rhamnosus may play a role in warding off mental disorders (Xu et al.; Romijn and Rucklidge). These probiotics could indirectly impact the development of mental illness by maintaining the intestinal barrier and reducing the incidence of intestinal inflammation, among other things, to alleviate the negative effects of mental illness, such as ecological dysregulation.



Conclusion

Because of these connections, the creation of stable gut communities that are advantageous to health is critical for the development and prevention of neurological diseases. As a result, looking for medicines that are favorable to gut health may be a more acceptable means of treating mental illness.

CONDUCTIVE HEART DISEASE

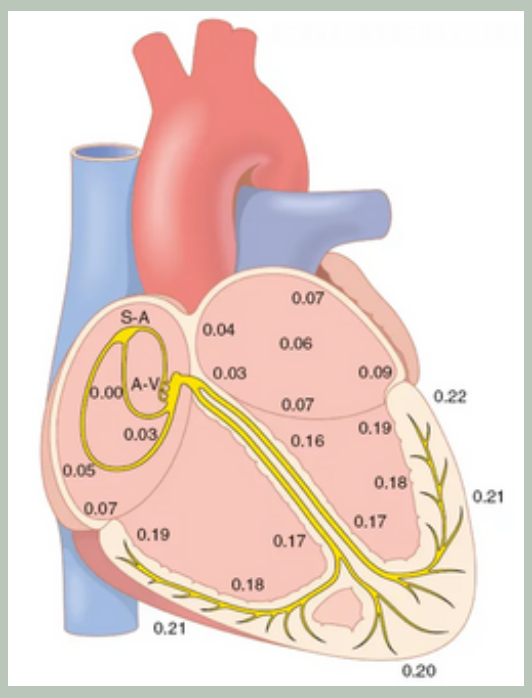
ZHIYUAN

SCI BUZZ >

There are many kinds of cardiovascular diseases with incidence rate and mortality ranking first among all diseases. It includes but is not limited to cardiac vascular disease, cardiac structure and function disease and conductive disease. The heart conduction system mainly includes sinoatrial node(SA node), atrioventricular node(AV node), atrioventricular bundle and Purkinje fibres, which are the basis for stimulating the heart beat at normal rhythm. The abnormality of any part causes dysfunction of cardiac conduction system. Thus affecting the normal physiological function of the heart, such as arrhythmia, bradycardia, ventricular tachycardia, etc. (Chinese People's Liberation Army General Hospital, n.d.)

CATEGORIES

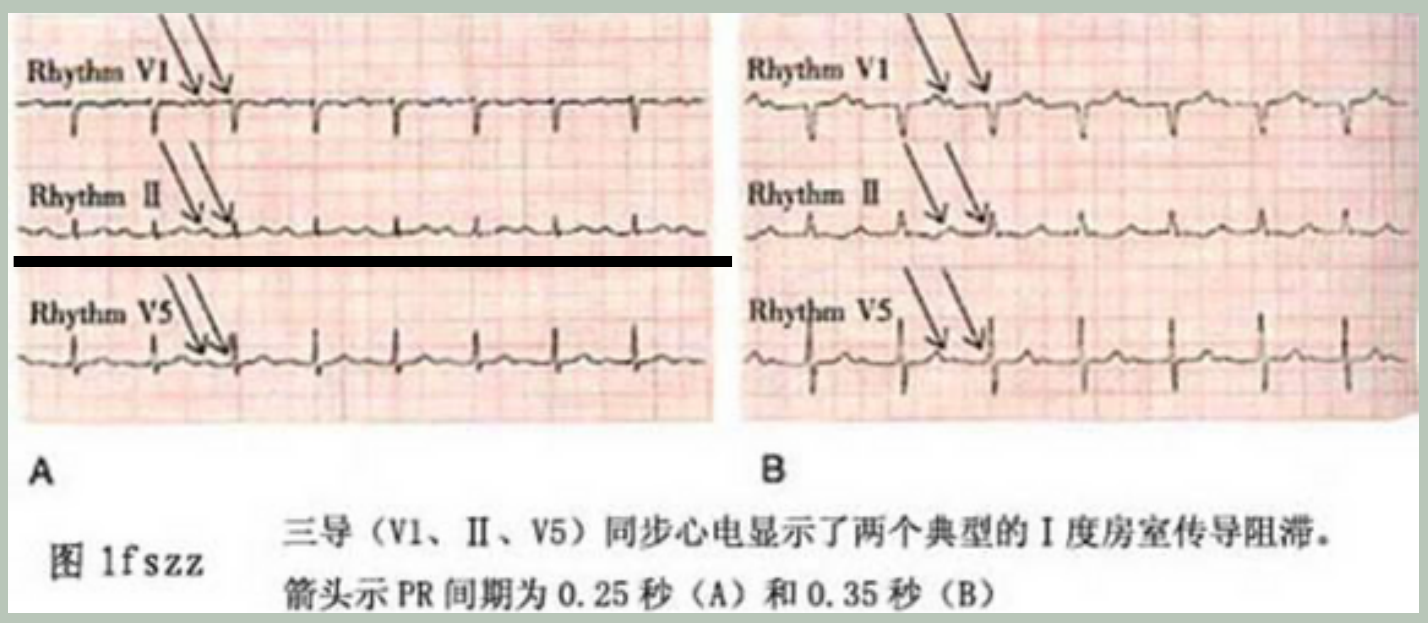
Cardiac conductive diseases can be divided into two major categories which are atrioventricular block (AVB) and intra-ventricular block(IVB). AVB refers to the delay or inability of conduction of SA node impulses to the ventricles after the physiological refractory period at atrioventricular junction area. AVB can occur in different parts of AV node, His bundle and branch of bundles. IVB refers to the conduction block below the bifurcation of His bundle. The intra-ventricular conductive system is composed of three parts: right bundle branch, left anterior branch and left posterior branch. The lesions of the intra-ventricular conductive system can be at a single branch, two branches or three branches (Beijing Chaoyang Hospital, n.d.).



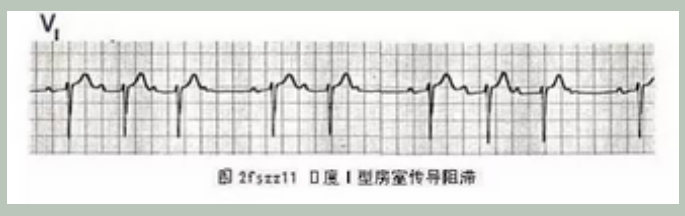
AVB can be further divided into first degree AVB, second degree AVB (type I & type II) and third degree AVB.

CLINICAL SYMPTOMS AND EXAMINATIONS

For AVB, patients with first degree atrioventricular block usually have no symptoms. During auscultation, the intensity of the first heart sound (S1) is reduced due to the extension of PR interval. Second-degree atrioventricular block can cause cardiac leakage, and some patients may have cardiopalmus. The electrocardiogram (ECG) shows that the SA node impulses could be transmitted to the ventricles but the PR interval was more than 0.20 seconds.



During auscultation, the intensity of S1 was gradually weakened and there was escape beat in degree-II AVB. ECG showed that firstly, the PR interval was gradually prolonged until a P wave was blocked and did not transmit to the ventricle. Secondly, adjacent RR intervals were progressively shortened until a P wave could not be transmitted down to the ventricle. Thirdly, including the blocked P-wave, the RR interval is twice smaller than the normal PP interval. Degree II type II AVB have escape beat as well but S1 strength is constant. The symptoms of degree three atrioventricular block (complete atrioventricular block) depend on the ventricular rate and progression of the disease.



The symptoms include tiredness, fatigue, dizziness, syncope, angina pectoris and heart failure. If complicated with ventricular arrhythmia, patient can have palpitation and feel discomfort. The PR interval of ECG is constant. However, when the first/second degree AVB suddenly progresses to complete atrioventricular block, the patients may suffer from temporary loss of consciousness or even convulsions due to cerebral ischemia caused by slow ventricular rate, which is called Adams-Strokes syndrome. Severe patients may even die. During auscultation, S1 intensity of third degree AVB often changes irregularly. S2 split can be either normal or abnormal. Resounding sound of S1 can be heard. When atrial and ventricular contractions occur at the same time, the jugular vein will have a
huge alpha wave. Due to the SA node impulses cannot be transmitted to the ventricles, the ECG manifestations are: 1) the activities of the atrium and the ventricles are independent and not related to each other; 2) Atrial rate is greater than ventricular rate; 3) The ventricular rate can be less than or equal to 40 times per minute according to different block sites.

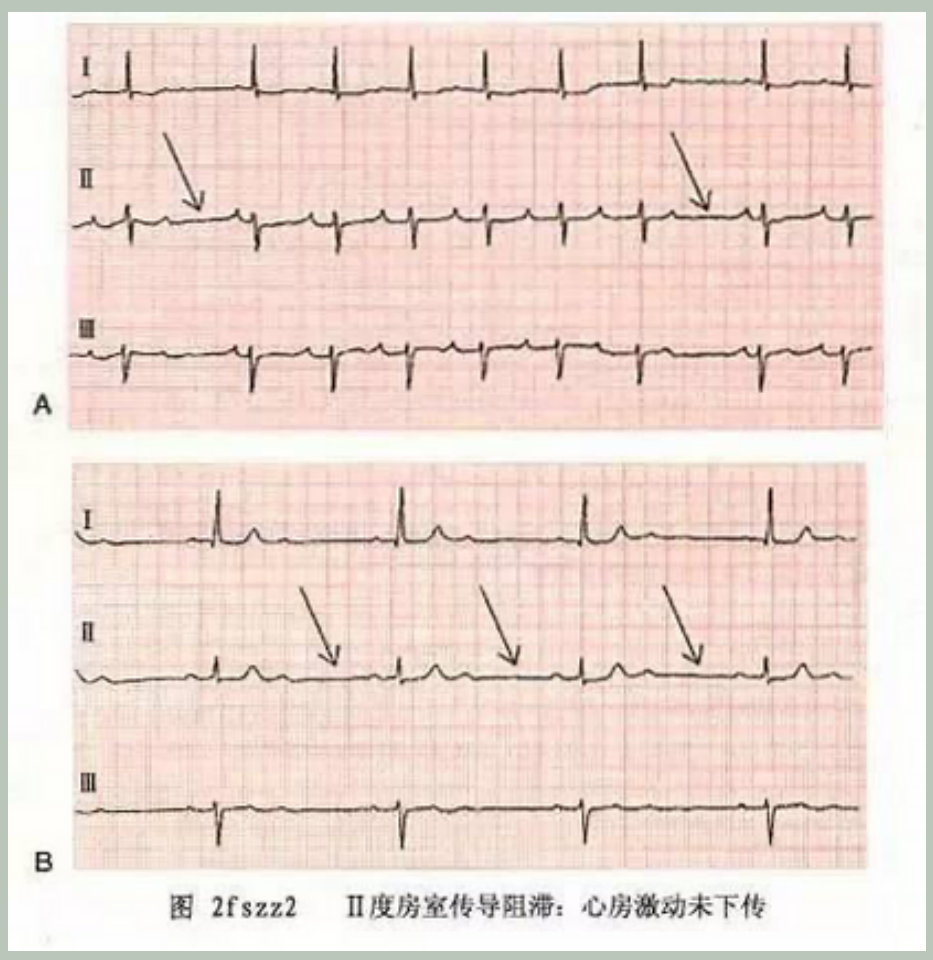


图 2fszz2　　Ⅱ度房室传导阻滞：心房激动未下传

For intra-ventricular block, complete and incomplete bundle branch block can be divided according to whether the QRS wave of ECG reaches 0.12 seconds. According to the block site, it is divided into left bundle branch block (LBBB) and right bundle branch block (RBBB). Single and double branch block usually has no clinical symptoms, but S1 and S2 split can be heard. In ECG, RBBB QRS ≥ 0.12s, lead V1-V2 showed rsR ', and R' wave was blunt. V5 and V6 are qRS and S-wave is wide. Direction of T wave is opposite to the main QRS wave. LBBB QRS ≥ 0.12s, V5 and V6 R waves are wide, with notch or blunt at the top, and no q wave in front.

V1 and V2 present broad QS wave or rS wave, and direction of T wave of V5 and V6 are opposite to main QRS wave. For left anterior branch block, lead I, aVL showed qR wave; II, III, aVF is rS-shaped, QRS<0.12s. Lead I and aVL showed rS wave of left posterior branch block; II, III, aVF showed qR wave and RIII>RII, QRS<0.12s. (Department of Internal Medicine, 2015).

ETIOLOGY, PREVENTION AND TREATMENT

It is very necessary to study the risk factors of cardiac conductive diseases. And, the recent cardiovascular health study published in the European Journal of Cardiology discussed this topic. In this study, we found that there were 257 degree-I AVB, 99 left anterior branch block, 193 RBBB, 76 LBBB and 102 patients with intra-ventricular block in 5050 subjects. After multiple variable adjustment studies, it was found that male patients with older age, higher BMI, hypertension and coronary heart disease were more likely to suffer from conductive heart disease. The prevalence rate of white people and those who do more physical exercise is lower (HR=0.91,95%CI 0.84-0.98, P=0.017) (Pubmed，2023)。 AVB is related to the increase of vagus nerve tension and previous diseases. Atropine 0.5-2mg intravenously and isoproterenol 1-4ug/min intravenously can be used in emergencies with AVB for patients with no cardiac pacing allowed. (Internal Medicine, 2015). If conditions permit, cardiac pacing should be given as soon as possible. For IVB, RBBB often occurs in patients with rheumatic heart disease, coronary heart disease and cardiomyopathy. LBBB often occurs in patients with congestive heart failure, acute myocardial infarction, and quinidine poisoning. In the treatment of IVB, artificial pacing should be taken when necessary.

THE RELATIONSHIP BETWEEN PSYCHOANALYSIS AND NEUROSCIENCE

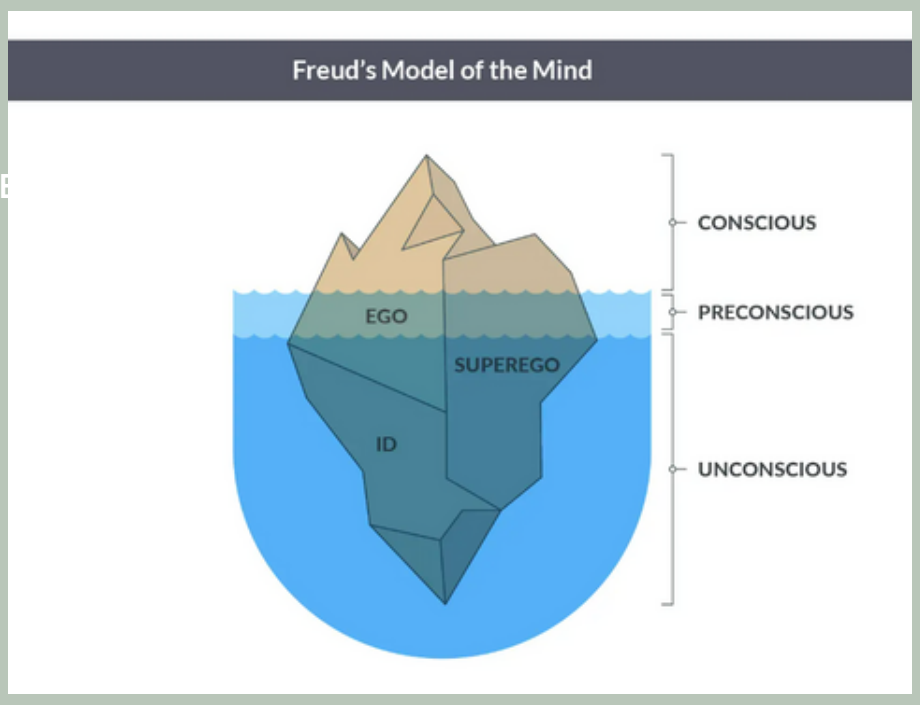
INTRODUCTION

It is no secret that the relationship between psychoanalysis and neuroscience has been contentious at best. Proponents of psychoanalysis argue that the study of neuroscience can provide a new understanding of mental processes and disorders. However, many psychologists and neuroscientists believe that psychoanalysis is an outdated approach and that it does not provide a good model for understanding cognitive processes in the brain. In this blog post, I will examine the strengths and weaknesses of psychoanalytic theory as they relate to current scientific research on brain structure and function.[1] I will also provide some recommendations for future research that will further our understanding of the relationships between psychoanalysis and neuroscience.

First, it is important to note that the methods used by modern psychoanalysts are essentially the same as that of contemporary scientists. For example, both scientists and psychoanalysts are guided by the scientific method in their respective studies. In addition, both practitioners and researchers rely on observable phenomena in their efforts to understand the human psyche. Both fields seek to discover truths that are repeatable and that can be substantiated by empirical data. Finally, both approaches are premised on the belief that the mind is not separate from the body and that the mind and body operate in a reciprocal relationship. Despite these similarities, there are significant differences between the two fields in terms of their theoretical frameworks and methods of inquiry. In particular, psychoanalysis focuses on interior mental states and experiences whereas modern science is focused on physical changes in the brain.

PRIMITIVE AND INSTICTUAL

One of the main tenets of psychoanalysis is that the mind cannot be separated from the rest of the body. According to Freud, the psychological structures of the mind are composed of "primitive" or "instinctual" drives that arise from the interactions between the body and the environment in which the individual lives. These unconscious urges direct the behavior of all people, including infants, adolescents and adults. In order to gain insight into the workings of the mind, Freud developed a theory of personality known as the psychosexual stages of development. This theory is based on the assumption that all human behavior can be explained in terms of the individual's interactions with his or her parents during early childhood. (Freudian theory assumes that biological and psychosocial forces shape behavior and determine an individual's personality. Psychoanalytic theorists argue that these forces are imprinted on the individual's unconscious mind, where they exert a powerful influence on his or her subsequent behavior.)[2]



TRIANGULAR THEORY

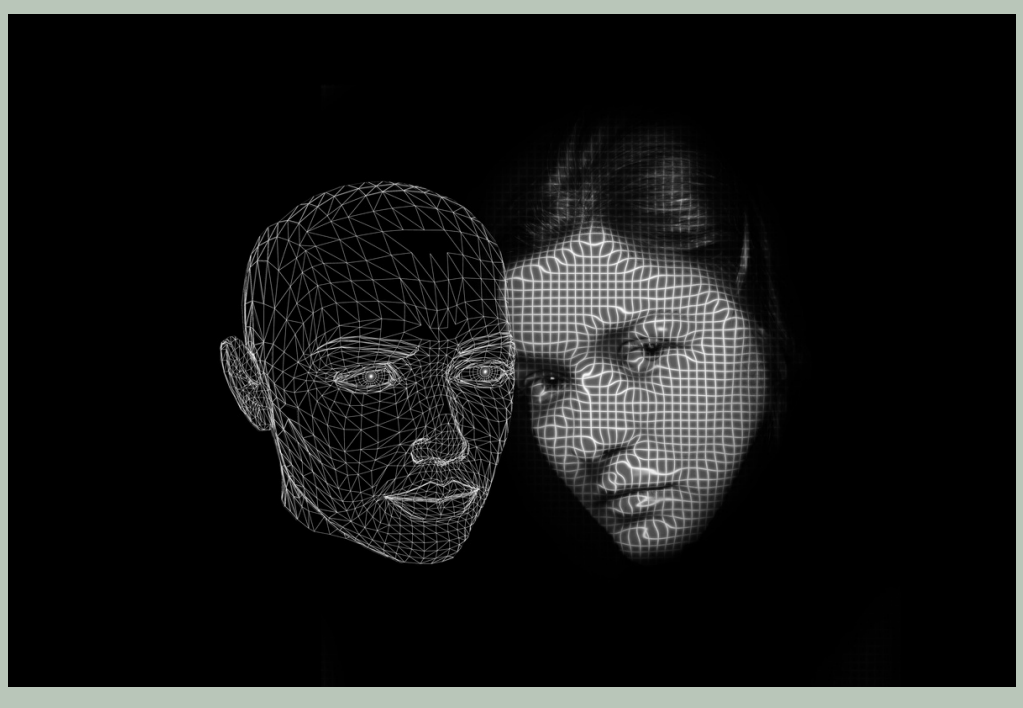
Drawing on the work of Freud and other psychoanalytic theorists, many contemporary psychologists have developed similar theories of personality. One prominent example of this approach is the triangular theory of personality developed by the psychologist John B. Watson in the early 1900s. The triangular theory of personality suggests that individuals form three important relationships with their parents during childhood: the loving/caring relationship, the demanding[3].

精神分析和神经科学的关系

众所周知，神经分析喝精神科学之间的关系充其量是有争议的。精神分析的支持者认为，神经科学的研究可以提供对心理过程和障碍的新理解。然而，许多心理学家争论神经科学的研究可以提供对于心理过程和疾病的新理解。

然而，许多心理学家神经科学家相信精神分析是一种过时的方法，他对于大脑认知进程的理解不会提供出一个好的模型。在这篇博文中，我讲会研究精神分析理论的优势和劣势，因为他们与当前关于大脑结构和功能的科学研究有关。

首先，最需要注意的是，现代精神分析学家使用的方法当代科学家的基本相同。例如，科学家和精神分析学家都由他们在各自研究的科学方法所引导。此外，从业者和研究学者都依靠可观察的现象来理解人类的心理。这两个领域都试图发现可重复的真理，这些真理可以通过经验数据得到证实。



最后，这两种方法都基于这样的信念，即心灵与身体并不分离，思想和身体处在一种相互的关系。尽管存在这些相似性，但在这两个领域中按照他们的理论框架和疑问方法，仍存在很大的不同。尤其精神分析聚焦于内部精神状态和体验，而现代医学侧重于大脑的物理变化。

精神分析的重要信条之一就是心灵不能与身体的其他部分分离。根据费洛伊德说法，心灵的心里结构由“原始”和“本能”驱动组成，这些渠东路来自身体与个体生活环境之间的相互作用。这些无意识的冲动知道这所有人的行为。包括婴儿、青少年和成年人。为了深入了解心灵的运作，费洛伊德发展出了一种人格理论，即性心理发展阶段。该理论基于以下假设，在童年早期个人与父母的相互互动为依据，所有的人类行为都可以被解释。（弗洛伊德理论假设生物和社会心理力量塑造行为并决定个人的个性。精神分析理论家认为，这些力量印在个人的潜意识中，在那里他们对他或她随后的行为产生强大的影响。）

利用弗洛伊德和其他精神分析理论家的工作，许多当代心理学家发展了类似的人格理论。这种方法的最突出例子就是心理学家约翰·B·沃森在1900年代提出的人格三角理论。人格三角理论提出个人在童年期间与他们的父母组成了三种重要的关系：爱/关怀关系、要求苛刻的关系。

SMART

vol. 2

authors: Katherine, Edith, Rachel

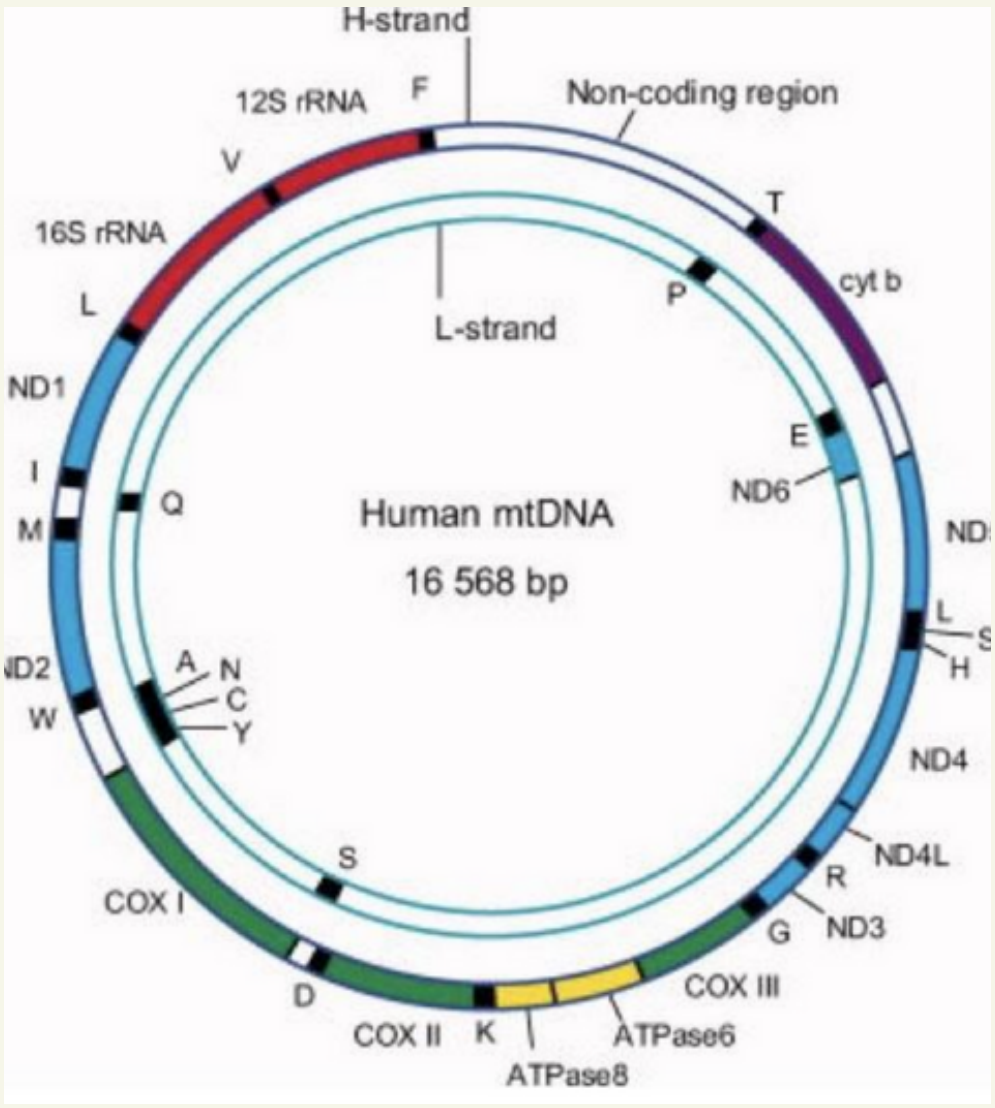
Background

Mitochondria, the organelles in eukaryotes, carry their own DNA. This DNA forms the mitochondrial genome, enabling the mitochondria to self-replicate and express the mitochondrial genes in the genome, and the proteins and enzymes encoded by the nuclear genes can be input into the cytoplasm for biological oxidation. Genomic and functional studies of mitochondria showed that mitochondria originated from purple photosynthetic bacteria. This kind of bacteria invaded eukaryotic organisms and formed endosymbionts in the cells, and then gradually degenerated into the present organelles, namely mitochondria. As early as 1996, Anderson et al. have determined the sequence of human mitochondrial genome. To date, the complete sequence of mitochondrial genomes of many animals and partial mitochondrial gene sequences of other animals have been determined. The study found that the base substitution rate of mitochondria is five to ten times faster than that of single-copy nuclear genome (genome in the nucleus). Therefore, mitochondrial DNA is a good molecular marker for systematic evolution. With regard to the research progress of mitochondrial genome replication and gene expression regulation, the enzymes and trans-acting factors involved in replication and expression have been found and isolated, and the mechanism of replication and expression regulation has been preliminarily understood. In short, mitochondrial genome is a noteworthy model system in molecular genetics and French biology.

According to the endosymbiotic theory, mitochondria were once bacteria that possessed their own DNA. After billions of years of evolution, they became organelles in eukaryotic cells, retaining a small portion of their DNA, while the remainder was transferred to the nucleus of the host cell.

Compared to human nuclear DNA, mitochondrial DNA (mtDNA) is relatively small, consisting of only 16,569 DNA base pairs and containing 37 genes. Of these genes, 13 encode essential components of the mitochondrial electron transport chain (ETC), responsible for producing the ATP energy required for cellular functions. Additionally, 22 tRNAs and two rRNAs found in mtDNA are involved in mitochondrial protein translation and ribosome formation, respectively.

One unique feature of mtDNA is its faster rate of evolution compared to nuclear DNA, making it useful for studying evolutionary history, human migration patterns, and the conservation of endangered species. By comparing the mtDNA sequences of different individuals or groups, scientists can determine relatedness and how long ago they diverged from a common ancestor.



Other differences between nuclear DNA and mtDNA
Nuclear DNA is linear, while mtDNA is circular.
Nuclear DNA is inherited from both parents, while mtDNA is inherited only from the mother.
One cell can only contain one nuclear DNA, while it can have a thousand mtDNA.
The noncoding DNA rate in nuclear DNA is 93%, while only three percent is mtDNA.

II mDNA replication and expression regulation

1. mDNA replication

The replication of animal mDNA is not restricted by the cell cycle. First, the LSP in the D-loop transcribes a portion of the RNA, which is cut off somewhere in the CSB region by RNA processing enzyme (mitochondrial RNA processing, Rnase MRP) to form the primer required for HI-strand replication, and then DNA polymerase Y (DNA polymerasey, DNA PoM) completes H-strand replication. The H-strand replication usually terminates at the TAS at the 5'-end of the D-loop, and a short segment of 7sDNA is then produced, which replaces the corresponding H-strand and pairs with the L-strand to form a three-stranded structure. When the replication fork of the H-strand moves to the OL, the L-strand starts to replicate. This shows that the replication of mDNA is much more complex than that of conventional mitosis.

Important proteins.

RNaseMRP, a nucleic acid endonuclease specific to the nucleus, whose function is to form the RNA primer for H-strand replication initiation and to recognize the conserved CSB sequences in the RNA transcribed by LSE

DNA polY: the only DNA polymerase present in mitochondria with DNA binding, 5'-)3" polymerization and 3)5 exonucleation functions. dna poly does not repair two common types of damage in mitochondria, desensitization and oxidative damage, and may be a cause of mutations.

Single strand binding protein (SSBP): Binds to the displaced single strand in the D-loop to prevent the single strand from forming a secondary structure of its own and preventing the DNA poy from working properly.

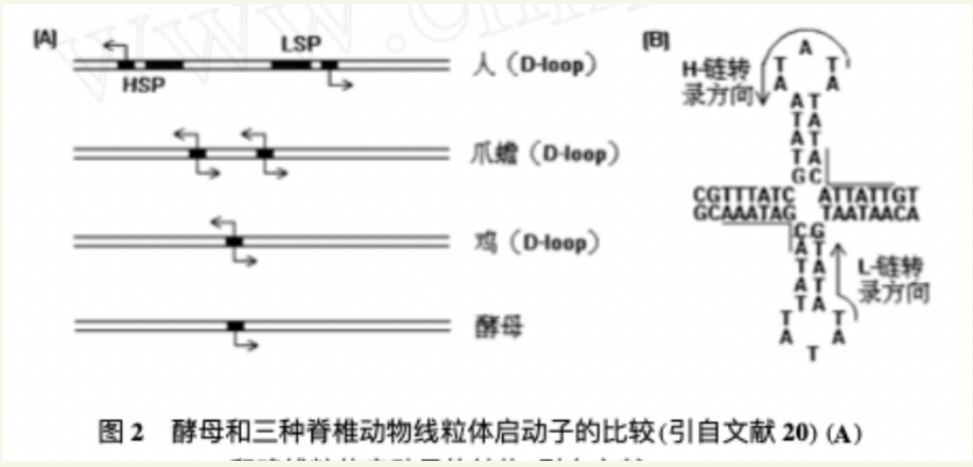


图 2　酵母和三种脊椎动物线粒体启动子的比较(引自文献 20) (A)

3. translation of mitochondrial protein genes

The mechanism is not clear, only one mitochondrial translation initiation factor has been identified, which is equivalent to prokaryotic initiation factor-2 (F-2) and is named as mitochondrial translation initiation factor-2, belonging to the GTPase family.

It acts mainly by binding to inactive mitochondrial F-2, which is converted to ADP in the presence of GTP and mRNA, and induces the binding of the initiating RNA to the small subunit of 28 ribosomes.

Review and prospect of genetic engineering drug research in China

There are two main problems in the research of genetic drugs in China: one is that there are too many copied drugs and not enough innovations. At present, the main efforts and support are focused on copying existing drugs. Although there are many generic drugs, there's only rhuIFNα1b as innovative drug in the market. Although the risk of copying is small and the speed is getting faster, there is the possibility of infringing intellectual property rights or patents. Therefore, blind imitation should be opposed. Instead, we should focus on imitating those whose patent is about to expire, has clear curative effects, and has broad application prospect. At the same time, we should carry out pioneering innovation and develop drugs through molecular design, controlled gene modification and gene synthesis. The second is too much repetition, low level performance and too much wasting of resources. Now there are many research and development efforts, the market is overheated, and the same kind of drugs are repeatedly developed. For example, there are 18 companies that study rhuG_CSF, and another 16 companies that study rhuGM_CSF. While there are too many companies studying these drugs, there are still many genetic drugs that have been found but are yet be researched and developed properly Therefore, we should develop genetic engineering drugs that are in phase I - II clinical trials and have definite therapeutic effects. At the same time, we should participate in international cooperation, seize opportunities and develop more and newer drugs.

2. mDNA transcription and post-transcriptional processing

Similar to prokaryotes, multiple cis-transons are transcribed and then post-transcriptional processing is performed to produce mature RNA

For example, the mitochondrial promoters of Xenopus laevis and chicken can be transcribed in both directions, with two bi-directional promoters found in Xenopus laevis and only one in chicken. For example, the mitochondrial promoters of Xenopus laevis and chicken can perform bi-directional transcription.

DNA polymerase.

The mRNA polymerase of the parent enzyme is the mtRNA polymerase encoded by the nuclear RPO41 gene, which has a weak and non-specific DNA binding ability, and together with scimtTFB can bind specifically to the promoter to form a transcription initiation complex, which can bend DNA. It is a cofactor for the formation of an active mRNAase holoenzyme.

The mitochondrial transcription system of Xenopus laevis also contains RNA polymerization and two transcription factors, xltTFA and xlmtTFB. xlhntTFA and h-mtTFA were eventually compared and found to contain a conserved C-terminal sequence that is required for stimulating transcriptional activity. It was also found that mtTFB may be required for transcription initiation, but not in humans, presumably because the human mtRNA polymerase has not been purified or because of the new organization of the human mitochondrial promoter during the evolutionary process. hmTEA was adapted to the new organization of the human mitochondrial promoter.

tRNA gene processing.

1. recognition of tRNA precursor by nucleic acid endonucleases. Cut off both ends of the sequence

2. add CCA sequence at the 3' end. 3.

citations

张方, 米志勇. 动物线粒体DNA的分子生物学研究进展[J]. 中国生物工程杂志, 1998, 18(3): 25-31,6.

Autoimmune diseases

Autoimmune diseases are disease states that result from an immune response by the body's immune system to its own components. The result of the body's immune response to foreign antigens is usually the elimination of antigens, and when the immune response to the antigen of its own cells or tissues, its cells or tissues are not easy to be completely eliminated by the effector cells of the immune system, but are constantly attacked, resulting in the body into a state of disease.
The causes of autoimmune diseases are not well understood. They are mainly caused by a combination of genetic and environmental factors. One theory is that some environmental factor, such as microbes or viruses, or drugs, may trigger changes that confuse the immune system and make people with related susceptibility genes more susceptible to disease.

Treatments and medications for autoimmune diseases:

Currently, there is no cure for autoimmune diseases, but only relief of symptoms. The goals of treatment are to reduce symptoms, control the autoimmune process, and maintain the body's ability to resist the disease. The drugs used to treat autoimmune diseases mainly fall into the following categories. Different drug indications are different, and the same drug can have multiple indications.

(1) Non-steroidal anti-inflammatory drugs:
By inhibiting cyclooxygenase (COX) and inhibiting arachidonic acid metabolism to produce prostaglandin, so as to have anti-inflammatory and analgesic effects. The main ones are:
Indole derivative: indomethacin
Propionic acid derivatives: ibuprofen, loxoprofen
Phenylacetic acids: dichlorophenolic acids
Cicam: Piroxicam, Meloxicam
Cyxib: Celecoxib
Non-acid: naphthalene bumethone
Sulfonyl anilines: Nimesulide

(2) immunosuppressants of chemical synthesis
Methotrexate (MTX) : dihydroreductase inhibitors that inhibit lymphocyte proliferation and inflammatory responses. Sulfasopyridine (SSZ) : inhibits white blood cell movement and reduces proteinolytic enzyme activity; Inhibit a variety of cytokines such as IL-6, IL-1a, IL-B, TNF, etc.
Azathioprine: inhibits lymphocyte proliferation, that is, prevents antigen-sensitive lymphocytes from transforming into immune mother cells and producing immune effects.
Tacrolimus: overinhibits the release of interleukin-2 (L-2) and comprehensively inhibits the action of T lymphocytes. Hydroxychloroquine sulfate: Antimalarial agent that stabilizes lysosome function by altering the intracellular acidic microenvironment; Inhibits the synthesis of TNF-α and INF-y, reduces the formation of autoantibodies and proliferation of lymphocytes.
Leflunomide: oxazoles derivatives that competitively inhibit dihydrolactate dehydrogenase activity and thus inhibit pyrimidine biosynthesis; Inhibits the activity of casein kinase, thus inhibiting the information transduction of inflammatory cells; And inhibit the activation of NF-kβ and the expression of INF-a and IF-1.
Cyclosporine: acts on the early activation process of CD4+ and inhibits the secretion of IF-2 and other cytokines; And inhibits cytokine-induced B cell activation.
Mycophenol ester: inhibits lymphocyte proliferation by inhibiting the activity of hypoxanthine nucleotide dehydrogenate (1MPDH) in the de facto purine synthesis pathway of lymphocytes.
Tofacitinib: A novel oral small-molecule JAK kinase inhibitor, tofacitinib can effectively inhibit the activity of JAK1 and JAK3 and block the signaling of a variety of inflammatory cytokines.

(3) Biologics
Some of the more common biological agents are the following:
① Cytokine targeting inhibitors
Cytokines (mainly TNF and BAFF) have been the main target molecules of biotherapy due to their important roles in autoimmune injury. Currently, monoclonal antibodies or recombinant cytokine receptors are used to inhibit the activity of inflammatory cytokines, but also inflammation-related or anti-inflammatory and immunosuppressive cytokines can be used.
Representative drugs: Infliximab, Adalimumab, Etanercept, Belimumab
② Targeting B cell antagonists
Cells not only produce antibodies in humoral immunity, but also present antigens to T cells to help regulate immune response. B-lymphocyte dysfunction is also one of the important causes of AID.
Representative drugs: Rituximab, orfamizumab
③ Targeted T cell antagonists
T lymphocytes have always played an important role in the occurrence and development of AID. Currently, targeted therapy of T cells is generally directed against T cell surface antigens to inhibit T cell activation and T-B cell interaction.
Representative drug: Abacipl
④ Complement activation inhibitor
Complement activation is an important marker of AID. It is through the cleavage of complement protein C5 to form inflammatory C5a molecules and cell membrane to attack complex C5b-9. Inhibition of C5 can block the formation of inflammatory mediators and thus reduce tissue damage.
Representative drug: Ekuzumab
In addition, biological agents are immunoglobulin, thymosin and so on.

(4) glucocorticoid
Glucocorticoid plays an important regulatory role in the development, growth, metabolism and immune function of the body. It is the most important regulatory hormone in the body's stress response. Commonly used are prednisone, prednisone, triamcinolone acetate and so on.
Organ specific AD versus systemic AD
AD can be divided into two main categories. The first type is organ-specific AD, Such as primary biliary cirrhosis (PBC), type 1 diabetes (T1D), and nervous system involved myasthenia gravis, MG), idiopathic membranous nephropathy (IMN) that attacks glomerular podocytes, and hyperthyroidism mediated by B and T cells. It is characterized by an immune response that is organ-specific when targeting autoantigens located within a certain organ and participating in the autoimmune process of the development of chronic inflammatory diseases. The second type is systemic AD, such as psoriasis with immune network imbalance, systemic lupus erythematosus (SLE), which involves multiple tissues and organs and may be caused by the systematic distribution of autoantigens.
Targeted drug therapy for systemic lupus erythematosus
SLE is a specific, chronic and damaging autoimmune disease. It generally involves many organs such as the kidneys, heart and brain. The main symptoms are red spots on the skin, joint pain, fatigue and deterioration of kidney function. Worldwide SLE population is mainly women of childbearing age, in patients with women are 10 times as many as men, the annual number of SLE in our country is about more than 1 million, with an increasing trend year by year.
With the gradual deepening of the pathogenesis of SLE and the rise of targeted therapy, the treatment program of SLE has been in an endless stream.
Targeted drug therapy for SLE is mainly divided into five targets including cytokines,B cells, T cells, Januskinase (JAK) and Bruton's tyrosine kinase (BTK).
Here we will introduce the use of B cell activator (BAFF, which is required for the development of B lymphocytes into mature plasma B cells). The target drug, belimumab, is a monoclonal antibody that acts on B cell activator. Belimumab has been approved by FAD for use in the treatment of SIE adult patients. Belimumab was approved by China's National Medical Products Administration and marketed in 2019. It is the first biologic agent approved for the treatment of SLE in the world.
Belimumab works by reducing B-cell activity when the immune system produces harmful 1g1-X antibodies that attack the body's own tissues. Belimumab binds to soluble BAFF in serum, preventing it from binding to receptors, thus inhibiting the proliferation and differentiation of B cells into antibody-producing plasma cells, leading to autoimmune B cell apoptosis, thus reducing the serum autoantibodies for therapeutic purposes.

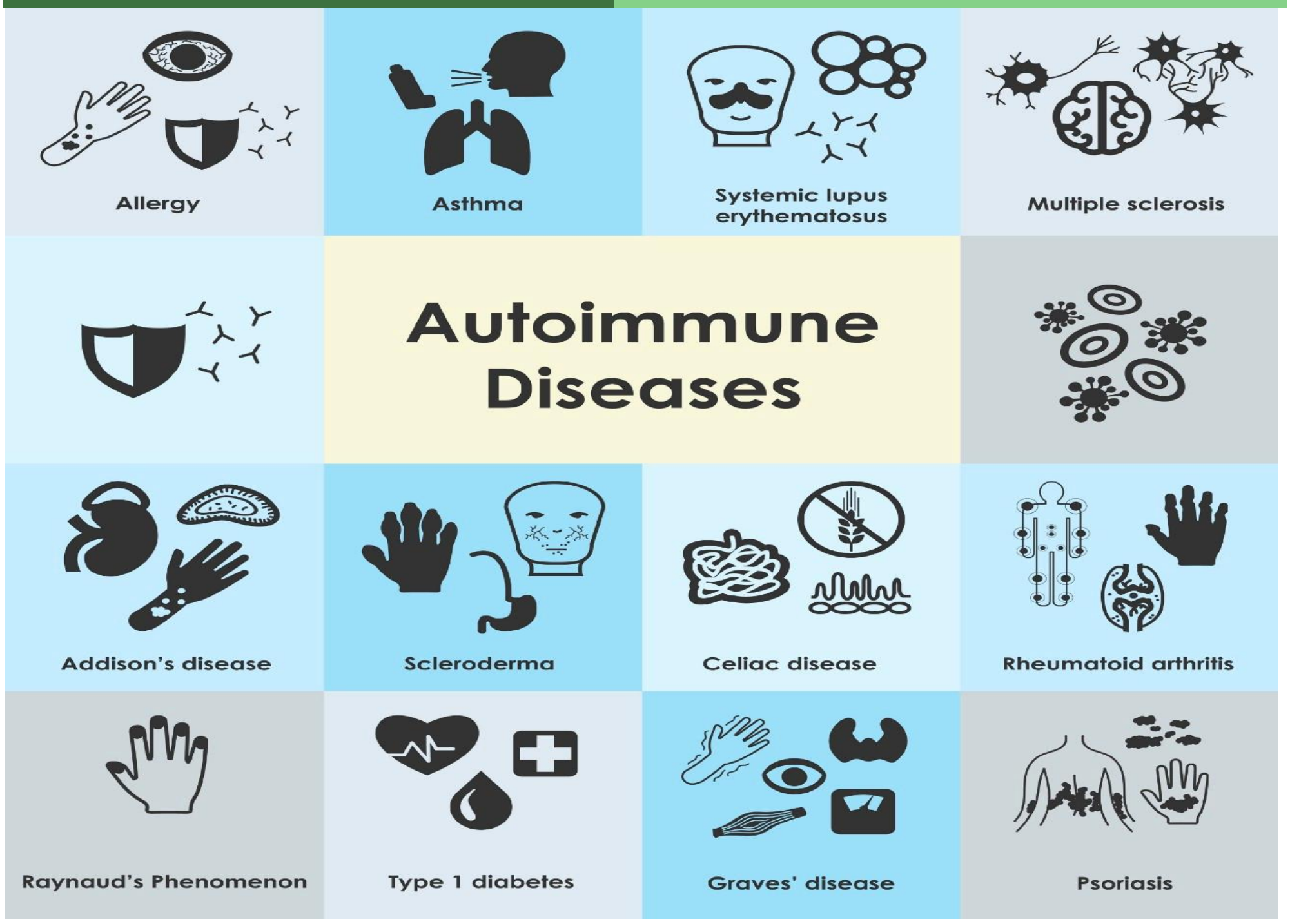
Belimumab is a long-term treatment that can take up to six months.

Autoimmune anemia

Autoimmune anemia is a group of diseases characterized by a malfunction of the immune system that leads to the production of autoantibodies that attack red blood cells as if they were foreign objects in the body. Autoimmune hemolytic anemia is a rare group of diseases that can occur at any age. Women are more common than men. The cause of half of these autoimmune hemolytic anemia is unknown (idiopathic autoimmune hemolytic anemia). Autoimmune hemolytic anemia can be caused by or associated with other diseases, such as systemic lupus erythematosus (lupus) or lymphoma, and autoimmune hemolytic anemia can also be attributed to the use of certain drugs such as penicillin.

The Puzzle of ulcerative colitis

AIn August 2020, Japanese Prime Minister Shinzo Abe announced that he was resigning as prime minister due to a recurrence of ulcerative colitis. Abe has reportedly suffered from ulcerative colitis since he was a teenager, indicating a lengthy pathology. It has repeated episodes and never recovers. Ulcerative Colitis is an inflammatory process that is confined to the mucosa and submucosa of the colon. The cause of ulcerative colitis is still unknown. There are many theories, but there is no firm conclusion at present. Ulcerative colitis is considered an autoimmune disease by some experts, who believe that the immune system mistakes "friendly bacteria" in the colon that aid digestion for a harmful infection, causing inflammation of the colon and rectum. Genetics can also affect the development of ulcerative colitis. If colitis runs in the family, the incidence of colitis in others will be greatly increased. For example, studies show that non-white patients are about 50 percent less likely than white patients.



2

CHINESE VERSION

English version is in the front

SMART magazine

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作者: Leona

词语

静脉注射：发生在静脉内的注射过程
抗氧化剂：一种能减缓因氧化而导致的腐败速率的物质。
氧化性：当一种物质与氧气或另一种氧化剂接触时发生的化学反应。

渐冻人口服药 Radicava ORS(依达拉奉口服混悬剂)

情况

肌萎缩性脊髓侧索硬化症（英语：Amyotrophic lateral sclerosis，缩写为ALS），俗称“渐冻症”，是一种渐进且致命的神经退行性疾病。肌萎缩侧索硬化症现今尚无根治方法。2022年5月，美国食品药品监督管理局（FDA）批准新药申请。其中包括三菱田边制药（MitsubishiTanabe Pharma）美国子公司MitsubishiTanabe Pharma America（MTPA）的RadicavaORS（edaravone，依达拉奉，口服混悬剂），用于治疗肌萎缩侧索硬化症。依达拉奉（edaravone）是一种自由基清除剂，被认为能够缓解氧化应激的影响，而这可能是ALS发病和病情发展的关键因素。目前该药物只能延缓病情进展，还没有能够治愈ALS的药物。

了解渐冻症

当说起前几年火爆全球的「冰桶挑战」时，我们可能会联想起一个罕见的疾病—渐冻症。

肌萎缩性脊髓侧索硬化症（英语：Amyotrophic lateral sclerosis，缩写为ALS），俗称“渐冻症”，是一种无法根治且致命的神经退行性疾病。著名的英国物理学家霍金就是患有该疾病，而他是渐冻症病例当中一个非常罕见的例子。因为大部分渐冻症患者的寿命大约为三至五年，而霍金与疾病对抗了55年，属实非常难得。ALS这个疾病会影响大脑以及脊髓的某些运动神经元，从而令运动神经元死亡。而由于运动神经会将大脑的信息传至肌肉，而神经元死亡导致信息无法传至肌肉，令到肌肉无法运动，一旦发生这种情况可能会造成肌肉无力、萎缩，而随着症状的加重会导致患者逐渐失去自主能力，就连吞噬都有困难，最后呼吸衰竭而死亡。整个过程就像被“冻住”一样，患者会在自己清醒的状态下，看着自己的行动机能逐渐地衰弱。

渐冻症的发病原因不明，而且任何人都有可能发病。可能是由于基因缺陷、遗传因素，或者是环境毒素暴露所影响等问题所造成。不过大致上可将ALS分为两种类型，分别是家族性和散发性的渐冻症。家族性的渐冻症即是有亲属患有ALS，但只占10%，而散发性即是没有亲属患有ALS。

“冰桶挑战(Ice Bucket Challenge)是一项筹款活动”

依达拉奉(Edaravone)是甚么?

由于渐冻症的不可捉摸性以及不确定性，至今依然没有任何药物可以有效地治疗ALS，但是有两种药物，分别是利鲁唑(Riluzone)以及依达拉奉(Edaravone)，可以有效地改善患者的生存状态以及缓慢病程发展。
依达拉奉(Edaravone)是一种脑保护剂（自由基清除剂），除了用于治疗ALS外，还可以治疗缺血性脑卒中。作用原理是基于自由基可以缓解氧化应激能力，防止脑细胞发生氧化损伤，其抗氧化能力可以保护神经系统，缓慢渐冻症的病程发展。

关于Radicava ORS

Radicava ORS是由三菱田边制药（MitsubishiTanabe Pharma）所研发的口服混悬剂，其美国子公司MitsubishiTanabe Pharma America（MTPA）于2022年5月获美国食品药品监督管理局（FDA）批准新药申请。依达拉奉(Edaravone)产品可分为静脉注射以及口服混悬剂，Radicava ORS属于口服混悬剂，而静脉注射以及口服混悬剂的成分以及作用原理是一样的。口服药物为患者提供了更大的便利，Radicava ORS所推出5毫升的便携装使患者可以把药物带回家吃，无需重新调配药物，同时药物无需冷藏，非常灵活且方便，唯一需要注意的地方是需要清晨空腹服用。

临床实验

在一项关键三期临床试验当中，对137名ALS患者以双盲安慰剂对照组的形式展开，试验全程以修订后的ALS功能评定表(ALSFRS-R)去评估Radicava对ALS的影响。而结果显示在治疗的第24周时，以Radicava去治疗的患者身体功能丧失下降了33%，相比起安慰剂起到了更好的效果。
在另一项为期24周的全球三期临床试验中，对185名ALS患者评估了Radicava ORS口服混悬剂的安全性以及耐受性，当中5%的患者有不良反应，包括肌肉无力、跌倒、疲劳、头痛等问题。

结语

Radicava ORS作为口服剂相比起静脉注射更为便捷，虽然现今还没有一种能完全治疗ALS的药物，但是Radicava ORS可以改善患者的生活质量，放缓病情的发展。至今科学家们对于AIS的成因还不是十分了解，而渐冻症有机会发生在任何一个人身上，所以我们最好的防范措施就是早发现、早诊断、早治疗。

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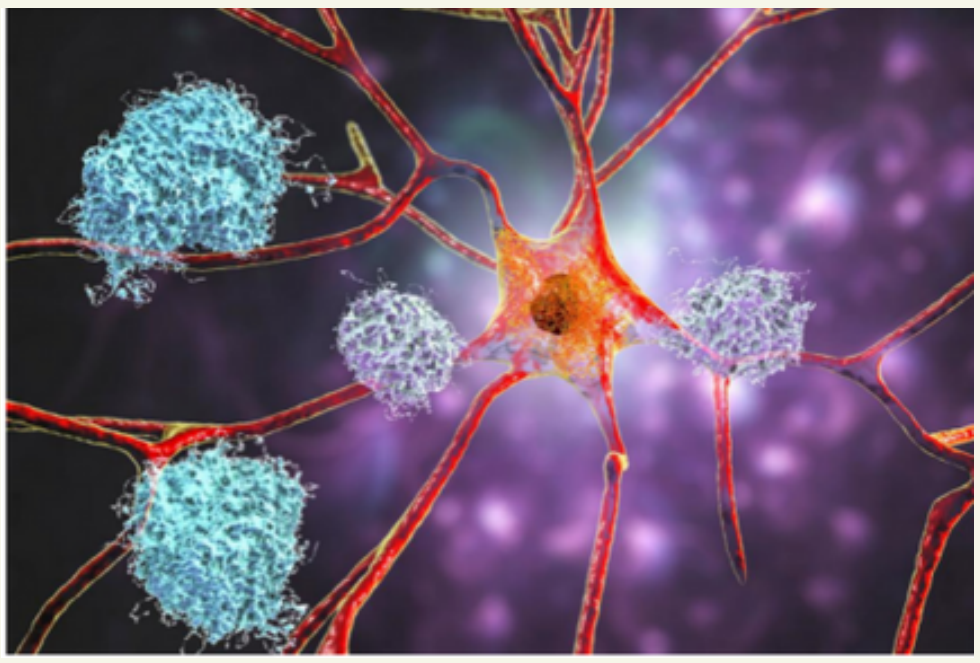
作者: *Sindy*

#1

黑暗的事实

根据疾病控制预防中,CDC，阿尔茨海默症也被称为不可逆的进行性脑部疾病痴呆。这类疾病开始伴随着轻度记忆力丧失，甚至最后会对周围的环境无能力交谈和反应。贯穿整个世界，这也是老年痴呆最常态化的一种疾病类型。阿尔茨海默症协会在他的文章“阿尔茨海默症的事实与数据”提供了进一步的信息。在这篇文章中，有超过500，000，000的阿尔茨海默症患者被估计，并且每三秒都会有一名患者发展为痴呆。更重要的是，研究表明阿尔茨海默症诊断的老年化正在衰减。

近期，阿尔茨海默症的杂志，一本在中国广为人知的杂志，成发现了一名19岁的患者被诊断为阿尔茨海默症。这篇文绽放就像一颗石头掷向了平静的水面，并搅起了数千层网络波浪。由于越来越多青年健忘的流行，使得“青年痴呆”也成为了社会的讨论话题。



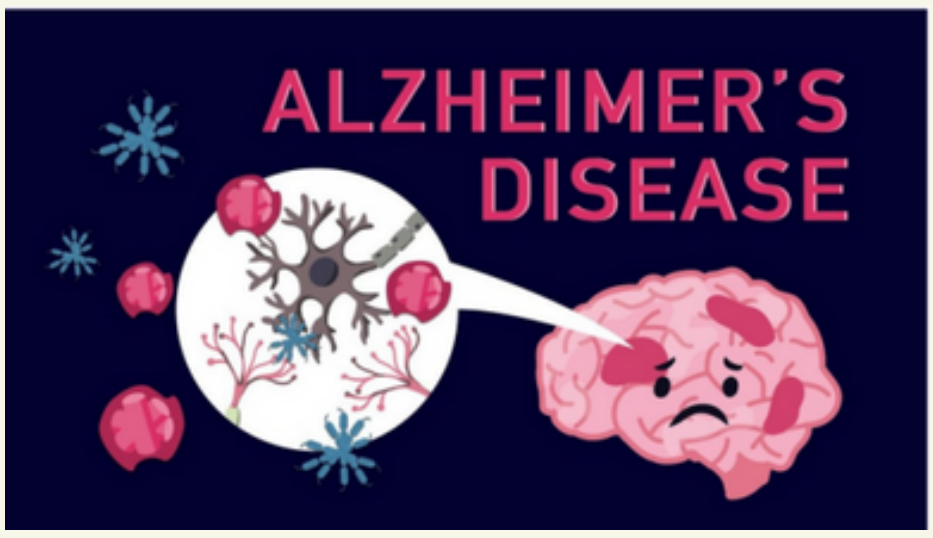
词汇库

阿尔茨海默症：一种先进的精神性疾病，它会破坏记忆和其它必须的机能

B-淀粉样蛋白：β-淀粉样蛋白的β亚基是一种由36-43个氨基酸组成的多肽，它主要负责在阿尔茨海默症患者的大脑中被发现的斑块

轻度认知功能障碍（MCI）：这是一种记忆和思考随年龄增长而与其衰减以及痴呆所导致的更多严重的衰退的阶段

现在我们理解它有多么重要了，所以让我们一起去寻找我们应该注意的科学信息吧!
阿尔茨海默症通过许多复杂的方式影响着人类的大脑，这需要多年的专业研究。但阅读这篇文章就可以让你很好的理解到它是如何工作的。在症状出现之前大脑的改变总是会开启，有可能在阿尔茨海默症的早期阶段就会看到大脑的有害变化。
β-淀粉样蛋白和tau缠结在大脑中积聚，神经元连接被破坏，中子失去功能。
当中子死亡，大脑的其他部分会萎缩并出现影响，导致阿尔茨海默症成为了绝症。这种损害似乎首先发成在海马体和内嗅皮层，这是大脑中负责记忆的部分，当阿尔茨海默症达到了最后阶段，这种破坏会扩散，大脑组织也会显著地萎缩。当患者的身体停止机能，患者可能会大多时间甚至整天卧床不起，直至死亡



#2

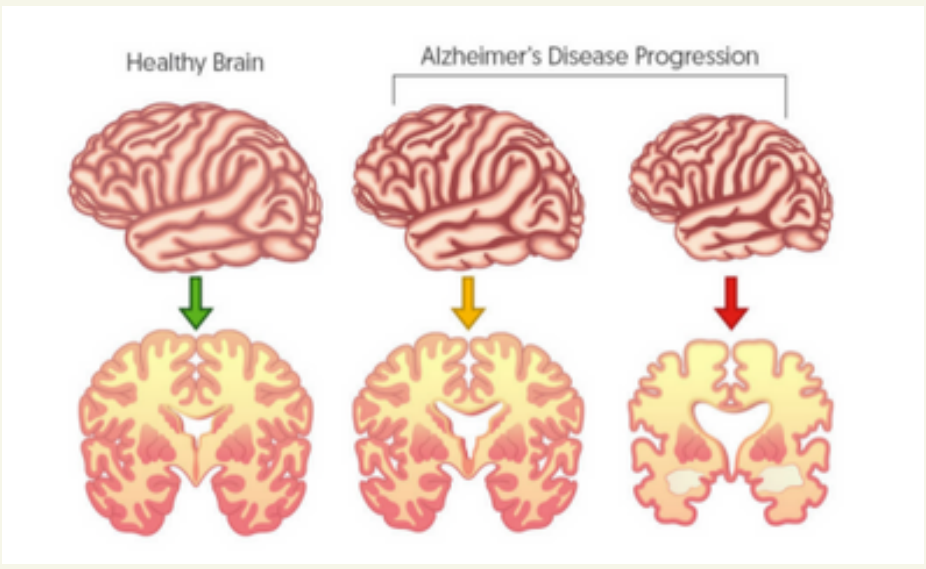
阿尔茨海默症又该怎样治疗呢?

如今没有现存的药物可以改变阿尔茨海默症的潜在疾病过程，因为人类的大脑是复杂的。目前，治疗主要聚焦在修复心里功能，疾病的炎症基础，以及管理行为症状。少数的干扰正在开发，并在多个临床测试。作为研究的一部分，疗法和非药物方法，正在被评估，非药物疗法包括身体运动、饮食、认知训练及其组合。

#3

药物突破

尽管一些药物有助于减少症状，并减轻特定的行为问题，然而，这些药物并不能改变疾病潜在程序。在一个限制时间里，他们对于一些（但并不是全部）患者有效。阿杜卡奴单抗（Aducanumab.）在该症状来临时，起着重要的作用。美国FDA（Food and Drug Administration）批准了阿杜卡奴单抗的加速批准途径。这一进程目的在于批准用于严重或危及生命的药物，以提供有意义的、由于目前治疗的治疗方案。这也是第一次被用来展示通过从患者的大脑移除β-淀粉样蛋白斑块有效地减缓阿尔茨海默症疾病的进程的药物，以减少早期阿尔茨海默症患者的认知和功能的下降。
阿杜卡奴单抗通过靶向识别并移除特定形式的储存在斑块中的β-淀粉样蛋白而生效，从而减少细胞死亡以及记忆领域的大脑组织丧失的可能。虽然大脑将会持续生成β-淀粉样蛋白，阿杜卡奴单抗也会同时对其进行削减。



#4

预防措施：

研究表明，遗传以外的多种因素都在阿尔茨海默症的发病原因中起作用。正在进行的研究将会帮助我们理解是否以及怎样·在我们的日常生活正做出一些改变从而减少患有阿尔茨海默症的风险。

这里有一些措施，你与你的家人可以进行练习，从而阻止阿尔茨海默症的发生。

1. 平衡饮食

为避免阿尔茨海默症，平衡饮食以及控制盐和肉的摄入非常重要。每天食盐摄入量不能超过10g,肉和糖也要保持最少量。

2. 适量运动

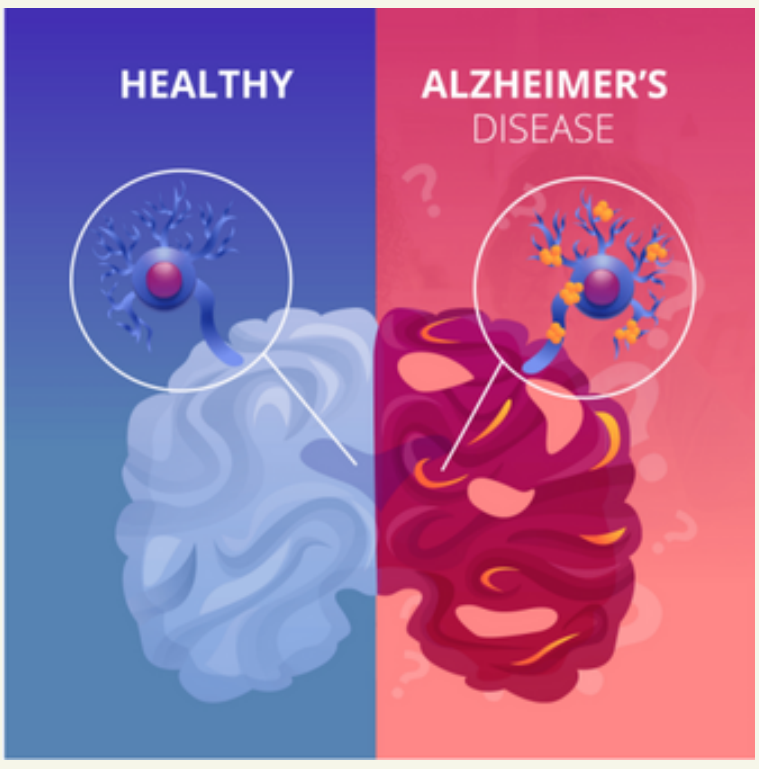
坚持锻炼也可以避免阿尔茨海默症，锻炼可以改善我们的免疫系统。手的运动也至关重要，你可以做一些简单的手指操来激发大脑。

3. 寻找医疗咨询

如果症状清楚，你应该去咨询医生，尽可能地避免进一步的危害。

#5

虽然变老并不等同于阿尔茨海默症，但是变老往往不是只是一个人，而是与整个家庭息息相关。老龄化不仅是对自我意识和如何规划我们生活的考验，也是对一个家庭严重的考验。
这需要我们尽可能早的去准备，从个人和家庭的观点去寻找它。我们希望我们可以对于父母的生理和心理状态上付出更多的关注，并将他们的年龄列入我们的生活计划中。除了关注生活细节外，带亲人定期体检也十分重要。



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SMART

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运动可以改变基因

Ray 刘子羽 & Olivia 钱书芸

摘要：六周的体育锻炼导致年轻男性骨骼肌细胞的表观遗传信息发生变化。这些变化发生在与疾病相关的基因组区域。科学家表示，他们的研究首次表明，运动如何重塑骨骼肌中的 DNA，从而建立新的信号以保持身体健康。DNA是存在于我们所有细胞中的分子指导手册。我们DNA的一些部分是基因，它是构建蛋白质（身体的组成部分）的指令，而其他部分被称为增强子，它调节哪些基因在何时开启或关闭，以及在哪个组织中。科学家们首次发现，锻炼会改变我们DNA中已知与疾病风险相关区域的增强子。

关键词：慢性病；糖尿病；胆固醇；易感受体；肾上腺素；GWAS 组蛋白；骨骼肌

一 、实验部分

人类身体中的基因，它们是构建蛋白质的指令，而其他特殊部分被称为增强子，它调节基因在何时启动表达。科学家们首次发现，锻炼会通过调节我们DNA中甲基化程度来改变相关区域的增强子。基因甲基化就是指DNA分子上CpG双核苷中的胞嘧啶（C）在酶的作用下选择性地添加甲基形成5'-甲基胞嘧啶的过程。CpG双核苷常位于基因转录调控区附近，其甲基化能引起染色质结构、DNA构象、DNA稳定性等发生改变，从而调控基因的转录和表达。低甲基化会一定程度上激活基因转录，超甲基化则会大概率让基因沉默。

科学家们招募了一些健康的25岁年轻人，让他们参加一个为期六周的耐力锻炼计划。

收集了他们在训练前后大腿肌肉的活组织切片，并检查了他们的DNA表观遗传特征是否在训练后发生了变化。

科学家们发现，在完成训练后，年轻人骨骼肌中有很多增强子的结构发生了一定的转变。他们通过将增强子和遗传数据库中的信息连接起来，发现了许多受调控的增强子已经被确定为个体间遗传变异的热点。

科学家们推测出运动对于一些远离肌肉的器官，比如说大脑有一定的良性影响，这可能是通过体液调节来实现的，同时进行一定的运动可以重塑骨骼肌中增强子，尤其是与认知能力相关的，这为科学家们提供了运动训练可以诱发大脑的分泌性肌肉因子的研究开展了新的方向。

结果显示，PGC-1α 、 PPAR-δ 和 PDK4 基因的去甲基化情况取决于运动的强度，研究发现，运动强度越大，其肌肉活检呈现出的去甲基化程度越高。

当启动子区的甲基化程度很高时，那么它与转录因子结合的可能性就比较小，转录因子是一种可以控制基因表达的蛋白质。也就是说，甲基化将会调节基因的表达。实验结果显示在锻炼后 PGC-1α 、 PPAR-δ 和 PDK4 这几个与能量代谢有关基因的表达都增强了。

此外，当培养的肌肉细胞被摄过多咖啡因时也会出现去甲基化。这是因为咖啡因会促进肌浆网释放钙质，而这会引起一定程度上的模拟肌肉收缩，所以钙质可能可以激活去甲基化。

二 基因

基因是产生一条多肽链或功能RNA所需的全部核苷酸序列。环境和遗传的互相依赖，演绎着生命的繁衍、细胞分裂和蛋白质合成等重要生理过程。生物体的生、长、衰、病、老、死等一切生命现象都与基因有关。基因存在于每个细胞的细胞核中，包含身体生长发育的信息。基因控制着你的身体的外观和功能，它们决定了你的身高。DNA是包含生物体制造蛋白质的指令的遗传蓝图。蛋白质对所有生命都是必不可少的，因为它们是大多数生物分子的组成部分。

三、体育锻炼的好处：

1.体育运动可以增强体质，提高抵抗力。

长期坚持运动可以增强心肺功能，改善血液循环，使机体气血畅通，加快体内废物排泄，促进机体新陈代谢。运动可以促进蛋白质合成，增强肌肉弹性，使人体骨骼肌的密度增加，增加关节的稳定性和伸展性，减少疾病。最经常运动的不吸烟的人，可使癌症的死亡率降低70%，即使经常运动吸烟的人，也可以使癌症的死亡率降低54%。不光是癌症、高血压、高脂血症的危险因子也可减少50%。

运动锻炼同样能够提高轻度认知障碍患者血浆中的簇集素水平，改善其认知能力和记忆力。运动也可以减少神经炎症，减轻脑损伤患者的症状。科学研究表明：运动，如：走路、跑步、弹琴、敲键盘、捡豆子等，可以有效刺激区域脑血流量，对预防和减缓老年痴呆都有帮助。而坐式生活的人比运动的人多出2倍患阿尔兹海默症的几率。

2.体育运动可以调节心情,振奋精神。

运动不产生快乐，但是会让人产生兴奋、刺激的感觉。虽然运动产生的多巴胺，和让我们快乐的多巴胺，产地不同，作用不同，但是这并不意味着运动就不能调节情绪。内啡肽是一种内成性的类吗啡生物化学合成物激素，它可以和吗啡受体结合，产生一种欣快感。当我们运动的时候，体内的内啡肽会持续分泌，这会让我们感到轻松愉悦、还能缓解压力。

在宏观层面体育运动以身体活动为基本手段，增强体质、增进健康及其培养人的各种心理品质为目的。尤其是随着社会经济的发展，人们的生活水平得到了提高，人们对精神方面的需要高于对物质方面的需要。人们对于体育的认识不只限于强身健体的方面，希望通过体育活动的参与得到更多的精神享受。不只是健身，更重要的是给人们的一种精神与神经方面的释放感，愉快感、成就感和心情的舒畅感。这些都是体育带给人们精神方面的价值。生活水平越高，人们越是注重体育精神层面的价值。

四、如何正确地运动

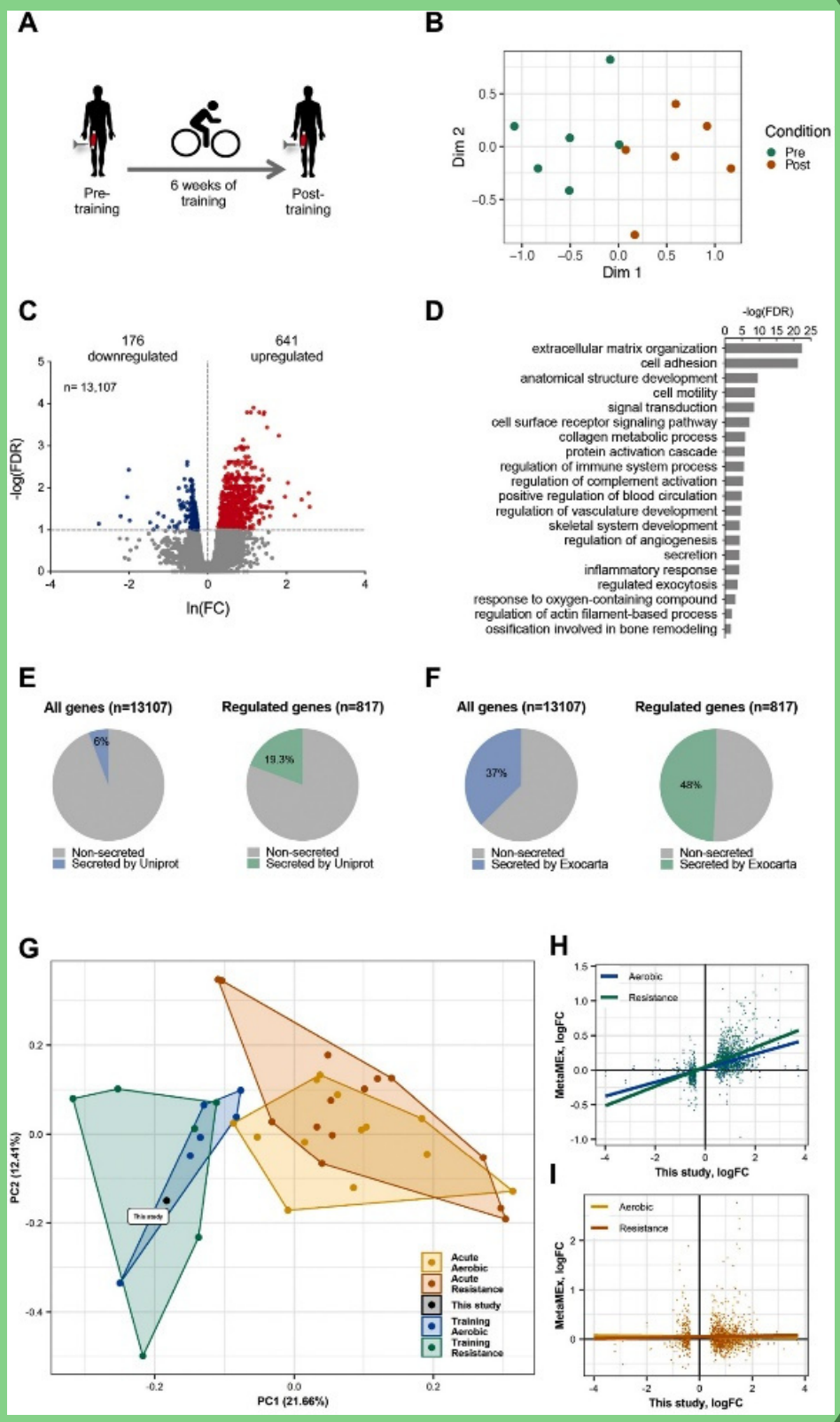
就减肥瘦身的有氧运动而言，建议是心率保持在60%~80%之间，刚好处于身体的舒适区边缘，每天活动半小时，就能产生极好的效果。

让自己保持做有氧运动时有些气喘的状态。比如跑步时，保持足够快的速度直到有些气喘，持续1~2分钟，然后改为快走，调整呼吸，重复即可。

想要获得更好的效果，最好结合复杂运动，如在10分钟的有氧热身之后练习瑜伽、舞蹈、体操、太极，等等，这些复杂的活动能让大脑的全部神经细胞参与其中。

五、结论

尽管现在发现运动可以改变基因，但我们还有很大的进步空间。运动对于我们每个人都是至关重要的，我们要做的是维持健康的身体，去创造更美好的世界。



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GUT-BRAIN AXIS AND MENTAL ILLNESS

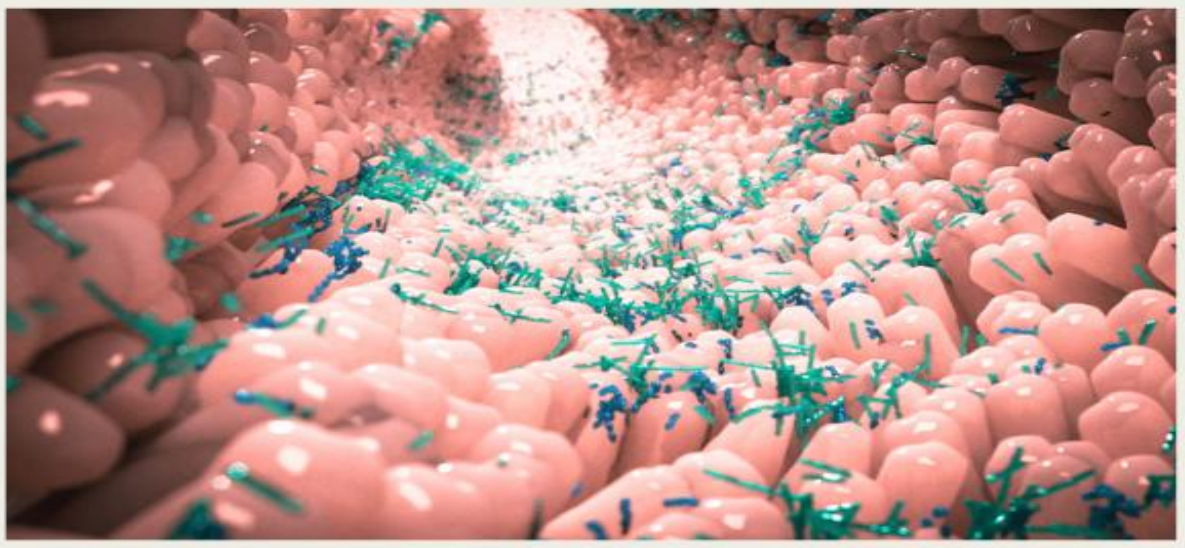
Abstract:

近年，发病率的上升让心理疾病备受关注。很多学者发现神经性疾病患者体内出现一系列胃肠道症状，尤其是肠道微生物具有一定的变化特点。本文针对脑-肠轴和精神性疾病间的关系做出探讨，并提出了利用其互相作用机制，通过改善肠道微生物菌群来间接影响精神性疾病的新思路。

Introduction

据心理健康的数据统计，近年心理疾病的人数增长，成为了很多人群的困扰。由于环境因素（持续高压力、气氛压抑和较少的运动等）的影响，尤其是在青少年人群中较为频发。从临床患者体现的发病机制，可以发现其不仅影响脑部，也对身体其他机能造成一定影响，尤其是消化道。

有各种实验表明，患有心理健康问题的实验对象具有一些胃肠道症状（便秘、呕吐、不适、腹痛、胀气）[1]。有学者提出这样的观点，肠道和大脑中具有一定的相关性。近期，很多学者以脑-肠轴的角度解释了精神疾病与肠道间的相互作用机制[2]。对精神疾病与脑-肠轴之间关系的探讨，可能为我们对缓解心理健康问题提供一个新思路



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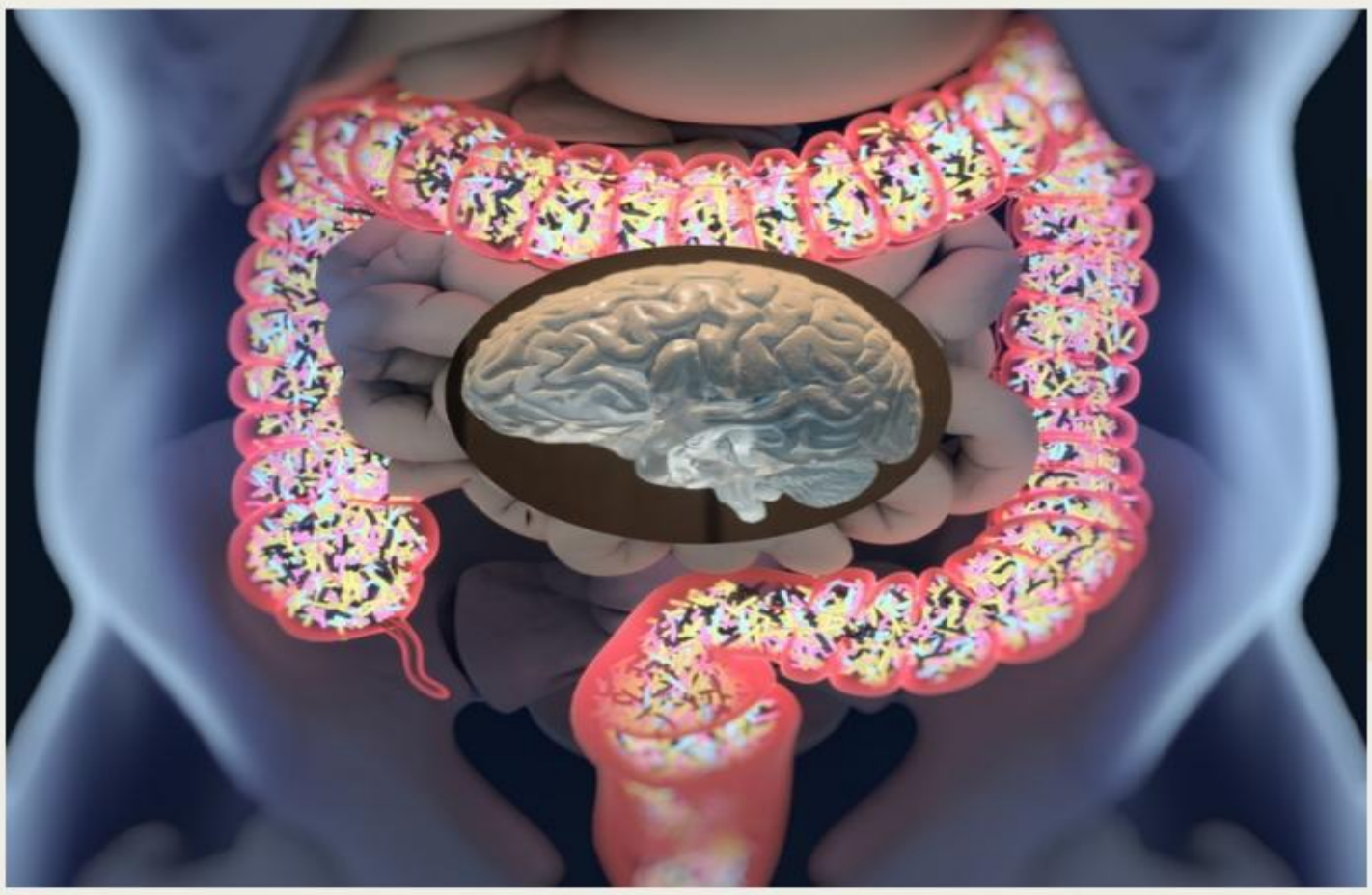
Discussion

肠道微生物群对人类的整体健康负有主要责任。很多文献中发现不同疾病可能出现不同的一定相似度的菌群变化[3,4]。因此，肠道微生物的变化是一种间接反应肠道健康的方式。神经系统疾病中出现的肠道微生物群变化已被报道[5]。有文献发现患有精神疾病的人表现出低多样性生态失调[6,7,8]。抑郁症患者的双歧杆菌和乳酸杆菌数量显着减少[9]。对于神经系统疾病，生态失调可能是危险因素[10]。肠道生态失调通过增加肠道屏障的通透性可能会触发炎症。饮食炎症与患精神系统疾病的风险增加有关。炎症的激活已被证明可以导致早期易感精神疾病的发生[11]。细菌也可能影响大脑功能和行为的观点似乎难以置信。近期，由于饮食引起的肠道细菌变化引起的炎症反应被发现可能会导致逆向促使情绪障碍的出现[12]。多样性的减少与多巴胺的产生有关[13]。肠道微生物群的多样性和稳定性的降低一定程度上决定了血清素的合成[14]。血清素（5-HT）、多巴胺（DA）和去甲肾上腺素（NE）等神经递质是被用作最常见治疗精神性疾病的药物。肠道微生物的失调抑制了有益于精神疾病改善的神经递质的产生，可能会对疾病进程带有负面影响。因此，针对患者体内的肠道微生物生态失调的治疗方式，可能是防止精神疾病恶化和改善精神疾病状态的有效方法。

GUT-BRAIN AXIS AND MENTAL ILLNESS

利用肠道微生物来影响精神疾病

肠道微生物对健康问题和神经精神疾病至关重要。饮食调整是一种改变肠道微生物的有效方式。不同的饮食会对微生物群的组成造成选择性的影响。有证据表明，不健康的饮食会造成肠道有益菌的减少和生态失调。精神疾病患者会产生选择性饮食行为，而由于这种行为引起的营养缺乏对精神疾病的发展有显着影响[15]。同时，恢复生态失调对相关精神疾病可能具有一定的缓解作用。肠道微生物的调节与有益菌和有害菌的平衡息息相关。在健康肠道中发现，常见的有益菌包括乳酸杆菌、双歧杆菌和鼠李糖乳杆菌等。



有临床实验证明，在益生菌的干预下，患者的精神疾病显著改善[16]。双歧杆菌、乳酸杆菌的特定菌株在大脑和行为中产生了积极的影响[17]。乳酸杆菌和双歧杆菌混合益生菌也有益于情绪的改善[18]。鼠李糖乳杆菌是预防精神疾病的有效物质[19]。喂养鼠李糖乳杆菌益生菌制剂的小鼠在精神疾病的测试中表现较好[20]。这些益生菌可以通过保护肠道屏障和降低肠道炎症的发生等方式，来改善因精神疾病导致的生态失调等不利影响，间接调整精神疾病的发展。

结论：

由于这些联系，产生对健康有益的稳定肠道群落对神经疾病发展和预防是至关重要的。因此，寻找对肠道健康有益的物质，可能是一种缓解心理疾病的接受度较强的方法。

心脏传导性疾病

ZHIYUAN

SCI BUZZ >

心血管疾病种类繁多，发病率及死亡率位列所有疾病之首。包括但不限于心 脏血管病变、心脏结构和功能病变以及传导系统方面的病变。心脏传导系统病 变，心脏传导系统主要包括窦房结、房室结、房室束以及浦肯野纤维网，他们 是使心脏以正常节律跳动的基础。任何一个部位出现异常，都可影响到心脏传 导系统，从而影响到心脏正常生理功能，如常见的心律失常、窦性心动过缓、 室性心动过速等（中国人民解放军总院，n.d.）。

分类

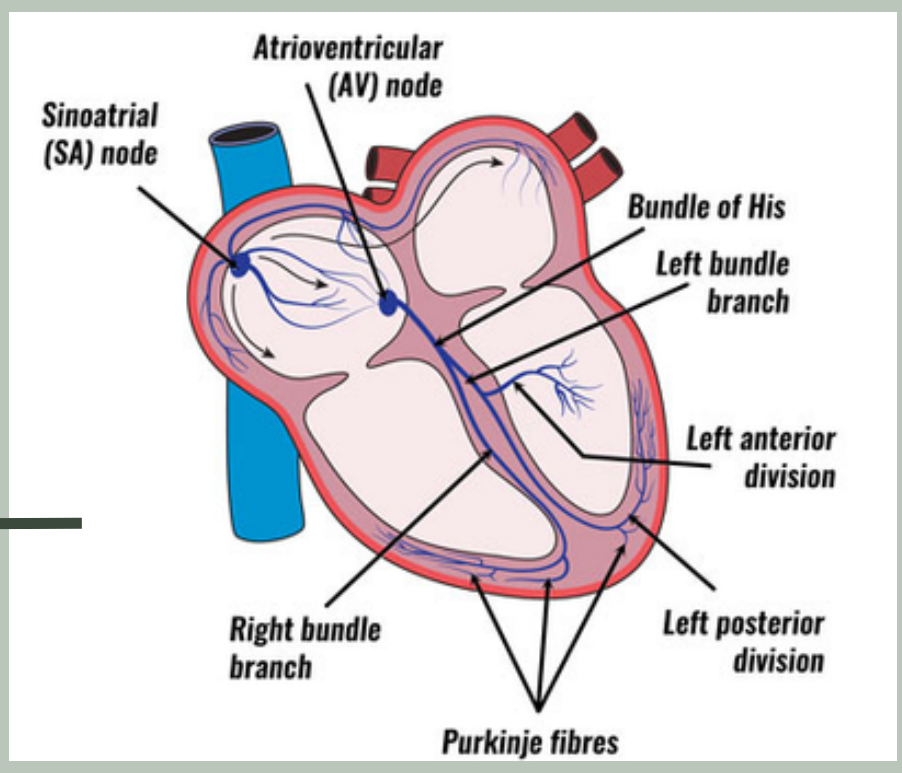
心脏传导性疾病主要可分为两大类，房室传导阻滞 （AVB）和室内传导阻滞（IVB）。AVB 是指房室交界区脱 离了生理不应期后，心房冲动传导延迟或不能传导至心 室。AVB 可以发生在房室结、希氏束以及束支等不同的 部位。室内传导阻滞是指希氏束分叉以下部位的传导阻 滞。室内传导系统由三个部分组成：右束支、左前分支
和左后分支，室内传导系统的病变可波及单支、双支或 三支（北京朝阳医院，n.d.）。AVB 可进一步分为一度 AVB， 二度 AVB（二度 I 型&二度 II 型）和三度 AVB。

临床表现及检查

对于 AVB，一度房室传导 阻滞患者通常没有任何症 状，在听诊时，由于 PR 间 期的延长，可闻及第一心音 （S1）强度减弱。二度房室阻滞可引起心搏脱漏，部分患者可有心悸症状。其心 电图（ECG）表现为心房冲动都能传导至心室， 但 PR 间期>0.20 秒。二 度 I 型 AVB 在听诊时可闻及 S1 强度逐渐减弱并有心搏脱漏。ECG 表现为一，PR 间期进行性延长，直至一个 P 波受阻没有下传到心室；二，相邻的 RR 间期进行性缩短，直至一个 P 波不能下传到心 室；三，包含受阻 P 波在内的 RR 间 期小于正常窦性 PP 间期的两倍。二 度 II 型房室阻滞亦有间歇性心搏脱 漏，但 S1 强度恒定。三度房室阻滞 （完全性房室阻滞）的症状取决于心 室率的快慢与伴随病变，症状包括疲倦、乏力、头晕，晕厥，心绞痛以及 心力衰竭。如合并室性心律失常、患 者可感到心悸不适。其 ECG 的 PR 间期恒定不变。然而，当第一度/二度 AVB 突然 进展为完全性房室阻滞，因心室率过慢导致脑缺血，患者可出现暂时性意识丧失，甚至抽搐，称为 Adams–Strokes 综合征，严重者有可能猝死。在听诊时，三度 AVB 的 S1 强度经常变化。S2 可呈正常或反常分裂。也可闻及响亮亢进的第一心音。心房与心室收缩同时发生时，颈静脉会出现巨大的 a 波。因其心房冲动均不能传导至心室，所以 ECG 表现为，1）心房 与心室活动各自立，互不相关；2）房率大于心室率；3）心室率可以根据不同阻滞部位小于或等于 40 次/分。

病因及预防和治疗

研究心脏传导性疾病的危险因素非常有必要，近期在欧洲心脏学杂志中发表的 心血管健康研究 CHS 探讨了这一话题。在这项研究中我们发现，5050 名受试者 中有 257I 度 AVB，99 名左前分支传导阻滞，193 名 RBBB，76 名 LBBB 和 102 名 室内传导阻滞患者。在多次变量调整研究后发现男性，年龄较大，BMI 较大，有
高血压，冠心病基础病患者更容易患传导病。而白人和较常做体力运动者患病率更低（HR=0.91，95%CI 0.84-0.98，P=0.017）（Pubmed，2023）。AVB 和迷走神经 张力增高，基础病有关，对因治疗是关键。阿托品 0.5-2mg 静脉注射，异丙肾上 腺素 1-4ug/分钟静脉滴注可用于 AVB 且无心脏起搏条件的紧急情况（内科学， 2015）。如条件允许，应尽早给予心脏起搏治疗。对于室内传导阻滞，RBBB 常发 生于风湿性心脏病，冠心病，心肌病的患者。LBBB 常发生于充血性心力衰竭，急性心梗，奎尼丁中毒的患者。治疗室内传导阻滞也重在对因治疗，必要时采取人
工起搏治疗。

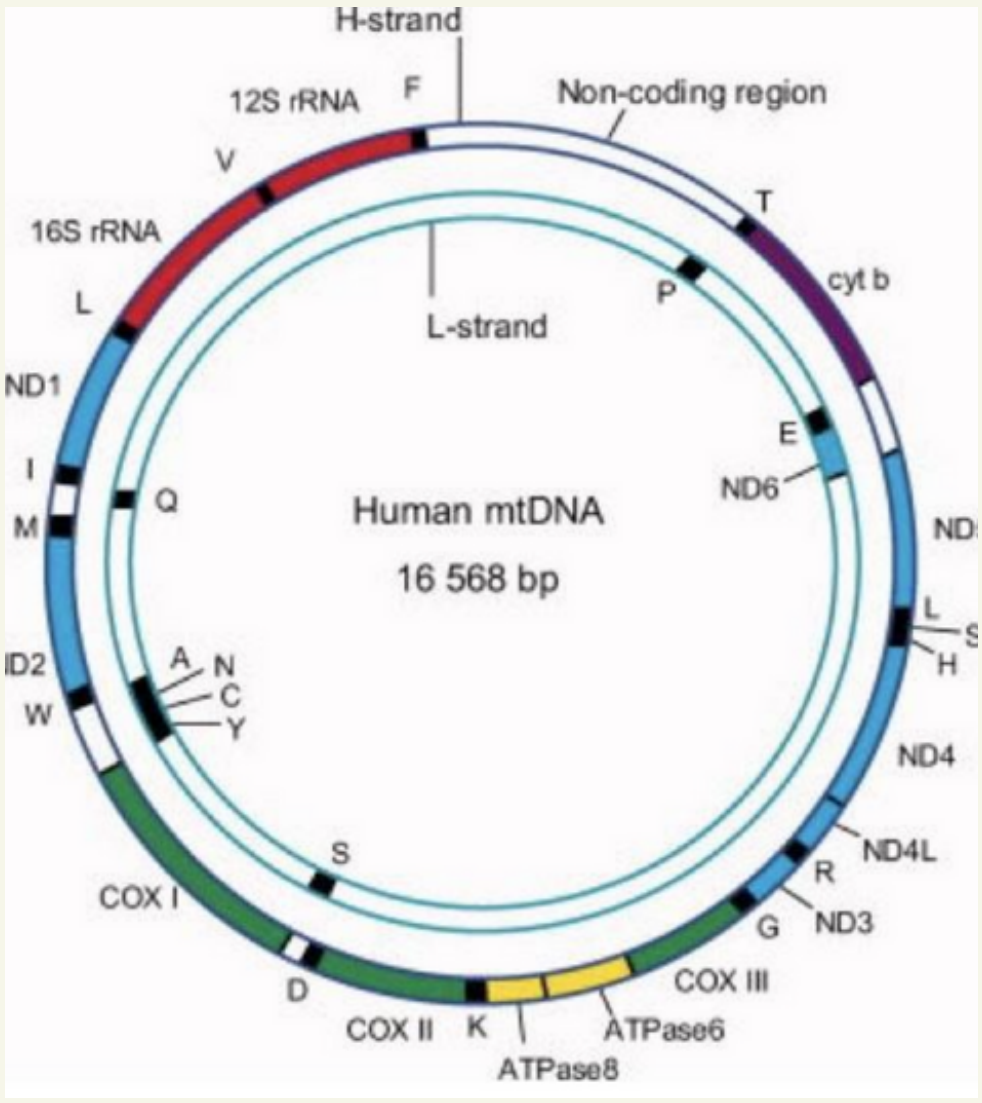


对于 IVB，可以根据 ECG 的 QRS 波是否长达 0.12 秒分为完全性和不完全性束支传导阻滞。根据阻滞部位分 为左束支传导阻滞（LBBB）、右束支传导阻滞（RBBB）。单支，双支阻滞通常无临 床症状，但间可听到 S1，S2 分裂。在 ECG 表现中，RBBB QRS≥0.12s，V1-V2 导 联呈 rsR'，R'波粗钝。V5，V6 呈 qRS，S 波宽阔。T 波于 QRS 主波方向相反。 LBBB QRS≥0.12s，V5，V6 R 波宽大，顶部有切迹或钝粗，前方无 q 波。V1，V2 呈宽阔的 QS 波或 rS 波形，V5，V6 T 波于 QRS 主波方向相反。左前分支阻滞 I， aVL 导联呈 qR 波；II，III，aVF 呈 rS 形，QRS<0.12s。左后分支阻滞 I 导联呈 rS 波；II，III，aVF 呈 qR 波且 RIII>RII，QRS<0.12s。（内科学，2015）。

SMART

vol. 2

作者: Katherine, Edith, Rachel



背景

真核生物中的细胞器——线粒体携带自己的DNA。这一DNA形成了线粒体基因组，使得线粒体可以自我复制和表达基因组上的线粒体基因，而核基因编码的蛋白质和酶可以输入细胞质，用于生物氧化。对于线粒体的基因组研究和功能研究表明线粒体起源于紫色光合细菌。这种细菌入侵真核生物，在其体内形成了内共生体，之后逐渐退化成现在的细胞器，即线粒体。早在1996年，Anderson等人就已经测定了人线粒体的基因组的序列。时至今日，多种动物线粒体基因组的全序列和一些动物的部分线粒体基因序列都已被测定。研究发现，线粒体的碱基替代率比单拷贝的核基因组（细胞核内的基因组）快五到十倍。因此，线粒体DNA是系统进化的很好的分子标记。关于线粒体基因组复制与基因表达调控研究进展，已经发现并分离了参与复制、表达的酶和反式作用因子，并且对复制与表达调控的机制有了初步认识。总而言之，线粒体基因组是分子遗传学和法语生物学研究中值得注意的模式体系。

一，

根据内共生理论，线粒体曾经是拥有自己 DNA 的细菌。经过数十亿年的进化，它们成为真核细胞中的细胞器，只保留了一小部分 DNA，而其余部分则转移到宿主细胞的细胞核中。

与人类核 DNA 相比，线粒体 DNA (mtDNA) 相对较小，仅由 16,569 个 DNA 碱基对组成，只包含了 37 个基因。在这些基因中，有 13 个编码线粒体电子传递链 (ETC) 的基本成分，负责产生细胞功能所需的 ATP 能量。此外，mtDNA 中发现的 22 种 tRNA 和两种 rRNA 分别参与线粒体蛋白质翻译和核糖体形成。

与核 DNA 相比，mtDNA 的一个独特特征是其演化速度较细胞核 DNA更快，这使其可用于研究进化历史、人类迁徙模式和濒危物种的保护。通过比较不同个体或群体的 mtDNA 序列，科学家可以确定相关性以及他们从共同祖先分离出来的时间。

細胞核DNA和mtDNA之间的其他差异核 DNA 是线性的，而 mtDNA 是环状的。核DNA遗传自父母双方，而线粒体DNA仅遗传自母亲。一个细胞只能包含一个核DNA，而它可以有上千个 mtDNA。核 DNA 中的非编码 DNA 率为 93%，而线粒体 DNA 只有 3%

二，MDNA 的复制和表达调控

mDNA 的复制

动物mDNA 的复制不受细胞周期的限制。首先，位于D-环的LSP 转录一部分RNA，由RNA 加工酶（mitochondrial RNA processing, Rnase MRP) 将此RNA 在CSB 区内的某处切断, 形成HI-链复制所需要的引物，然后由 DNA 聚合酶Y (DNA polymerasey,DNA PoM) 完成H-链的复制。H-链的复制通常终止在D-环 5'-端的TAS 处，随后产生一段短的7sDNA，并代替相应的H-链与L-链配对,形成一个三链结构。当H-链的复制叉移动到OL处时, L-链才开始复制。由此可见，mDNA的复制相比与传统的有丝分裂复杂的多。

- 重要蛋白质：

RNaseMRP，是细胞核中特异性的核酸内切酶，其功能是形成H-链复制起始的RNA 引物，识别由LSE转录出的RNA 中保守的CSB 序列

DNA polY：线粒体中存在的唯一的DNA 聚合酶，具有DNA结合、5'-)3”聚合和3)5外切功能。DNA poly对线粒体中两种常见的损伤一脱感基损伤和氧化损伤的修复功能不强，可能是导致基因突变的原因之一。

单链结合蛋白(SSBP)：结合于D-环中被置换出的单链上,以防止单链自身形成二级结构而阻碍DNA poy正常工作。

mDNA 的转录与转录后加工

与原核生物类似，转录出多顺反子，再经过转录后加工过程生成成熟RNA脊椎动物彼此之间的线粒体存在一定差异，例如爪蟾和鸡的线粒体启动子可以进行双向转录, 爪蟾中发现两个双向启动子,鸡中只有一个。共同点是都具有HI-链启动子区和L-链的转录起始位点，都可以进行双向展露，只是形态和数量上具有一定区别。

DNA聚合酶：

酶母的mRNA 聚合酶为核RPO41基因编码的mtRNA 聚合酶，具有弱且非特异的DNA 结合能力,与 scimtTFB一起能和启动子特异结合,形成转录起始复合物, 可使DNA 弯曲。并在转录启动后不久释放scmtTFB.是形成有活性的mRNA酶全酶的辅助因子。
爪蟾的线粒体转录体系也含有RNA 聚合离和两个转录因子xltTFA、xlmtTFB。最终通过对比xlhntTFA 和h-mtTFA发现其都含有一保守的C-端序列，为刺激转录活性所必需。同时发现mtTFB 可能是转录起始的必需因子，但人并不具有，推测是犹豫人的mtRNA 聚合酶还未纯化或是因为在进化过程中.hmTEA适应人线粒体启动子新的组织方式。

tRNA 基因加工：

1. 核酸内切酶识别 tRNA 前体.切去两端序列
2. 在3’端加上CCA 序列。

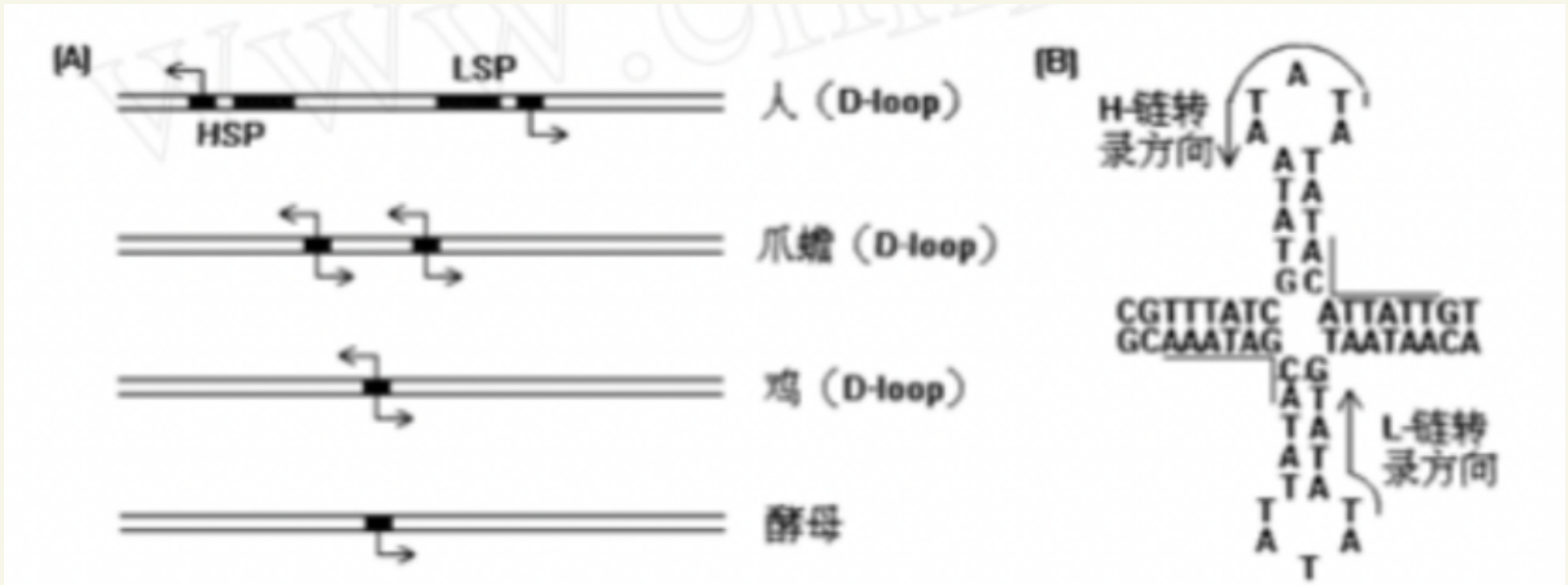


图 2　酵母和三种脊椎动物线粒体启动子的比较(引自文献 20) (A)

线粒体蛋白质基因的翻译

机制尚不明确，目前只有一个线粒体翻译起始因子被鉴定, 其作用相当于原核生物的起始因子-2(F-2),被命名为线粒体翻译起始因子-2,属于 GTP 酶家族。
作用主要通过与无活性的线粒体 F-2结合，GTP 和mRNA存在的条件下转换为ADP，促使起始 RNA 与 28核糖体小亚基结合。

引用

张方, 米志勇. 动物线粒体DNA的分子生物学研究进展[J]. 中国生物工程杂志, 1998, 18(3): 25-31,6.

三，我国基因工程药物研究回顾与展望

我国基因药物研究主要存在两个问题：其一是仿制过多，而创新不够。现在主要的努力和支持集中在仿制已有药物上。造成虽有许多仿制药物，而上市药物中只有rhuIFNα1b为首创药物。虽然仿制风险小，速度也越来越快，但存在侵犯知识产权或专利的可能性。因此应当反对盲目仿制，重点仿制专利即将到期，疗效明确，应用前景广阔的药物。同时进行开拓性创新，通过分子设计，有控制的基因修饰及基因合成研发药物。其二是重复过多，水平不高，浪费太大。现在有许多研究与开发，市场过热，重复研制同一类药物。例如，研发rhuG_CSF的有18家公司，研究rhuGM_CSF的也有16家公司。而在研究这些药物的公司过多的同时，尚有众多已发现基因药物有待研究开发。因此，应开发处于I-II期临床，有确切疗效苗头的基因工程药物。同时，参与国际合作，抓住机遇，开发更多更新药物。

自身免疫性疾病

自身免疫疾病是因机体免疫系统对自身成分发生免疫应答而导致的疾病状态。机体对外来抗原发生免疫应答的结果通常是抗原的清除,而对自身细胞或组织抗原发生免疫应答时,自身的细胞或组织不易被免疫系统的效应细胞完全清除而是不断地受攻击,结果使机体进入疾病状态。自身免疫性疾病的发病原因尚不清楚。主要是遗传和环境因素的共同作用导致的。有理论认为是一些微生物（如细菌或病毒）或药物等环境因素可能引发混淆免疫系统的变化，使携带相关易感基因的人更倾向于患病。

自身免疫性疾病的治疗方式和药物：

目前自身免疫性疾病还无法治愈，只能缓解症状，其治疗的目标是：减轻症状、控制自身免疫过程、保持身体抵抗疾病的能力。治疗自身免疫性疾病的药物主要有以下几类，不同的药物适应症不同，同一药物可以有多种适应症。

（1）非甾体类抗炎药：

通过抑制环氧化酶（COX）而抑制花生四烯酸代谢产生前列腺素，从而具有抗炎镇痛等作用。主要有：

吲哚衍生物：吲哚美辛

丙酸衍生物：布洛芬、洛索洛芬

苯乙酸类：双氯酚酸

昔康类：吡罗昔康、美洛昔康

昔布类：塞来昔布

非酸类：萘丁美酮

磺酰苯胺类：尼美舒利

（2） 化学合成类免疫抑制剂

甲氨蝶呤（MTX）：二氢还原酶抑制剂，抑制淋巴细胞增殖和炎症反应。

柳氮磺吡啶（SSZ）：抑制白细胞移动，降低蛋白溶解酶活性；抑制多种细胞因子如IL-6、IL-1α、IL-β、TNF等。

硫唑嘌呤：抑制淋巴细胞的增殖，即阻止抗原敏感淋巴细胞转化为免疫母细胞，产生免疫作用。

他克莫司：过抑制白介素-2（L-2）的释放，全面抑制T淋巴细胞的作用。

硫酸羟基氯喹：抗疟药，通过改变细胞内酸性微环境稳定溶酶体的功能；能抑制TNF-α、INF-γ的合成，减少自身抗体的形成和淋巴细胞的增殖。

来氟米特：恶唑类衍生物，竞争抑制二氢乳酸脱氢酶活性，从而抑制嘧啶的生物合成；抑制酪酸激酶的活性，从而抑制炎细胞的信息传导；抑制NF-κβ的激活，阻止INF-α、IF-1的表达。

环孢素：作用于CD4+早期活化过程，抑制IF-2和其他细胞因子的分泌；还可抑制细胞因子诱发的B细胞活化。

麦考酚酯：抑制淋巴细胞嘌呤从头合成途径中次黄嘌呤核苷酸脱氢酸(IMPDH)的活性，从而抑制淋巴细胞增殖的作用。

托法替尼：新型口服小分子JAK激酶抑制剂，托法替尼可有效抑制JAK1和JAK3的活性，阻止多种炎性细胞因子的信号传导。

（3）生物制剂

比较常见的生物制剂有以下这些：

① 细胞因子靶向抑制剂

细胞因子(主要是TNF和BAFF)，因其在自身免疫损伤中的重要作用而一直是生物治疗的主要靶分子。目前，主要是通过单克隆抗体或者重组的细胞因子受体来抑制炎性细胞因子的活性，当然也可利用炎症相关或有抗炎和免疫抑制作用的细胞因子进行治疗。

代表药物：英夫利昔单抗、阿达木单抗、依那西普，贝利木单抗

② 靶向B细胞拮抗剂

细胞不仅能在体液免疫中产生抗体，还能提呈抗原给T细胞，帮助调节免疫反应，B 淋巴细胞功能障碍也是导致AID的重要原因之一。

代表药物：利妥昔单抗、奥法木单抗

③ 靶向T细胞拮抗剂

T淋巴细胞在AID的发生发展中一直扮演很重要的角色，目前T细胞的靶向治疗一般是针对T细胞表面的抗原来达到抑制T细胞活化及T-B细胞相互作用的目的。

代表药物：阿巴西普

④ 补体活化抑制剂

补体激活是AID的一个重要标志，是通过补体蛋白C5裂解来形成炎性C5a分子和细胞膜攻击复合C5b-9的，抑制C5可以阻断炎性介质的形成从而减少组织损害。

代表药物：依库珠单抗

此外，生物制剂还有免疫球球蛋白、胸腺肽等。

（4）糖皮质激素

糖皮质激素对机体的发育、生长、代谢以及免疫功能等起着重要调节作用，是机体应激反应最重要的调节激素，常用的有泼尼松、泼尼松龙、醋酸曲安奈德等。

器官特异性AD与系统性AD

AD可分为两大类，第一种类型是器官特异性AD，如原发性胆汁性肝硬化（primary biliary cirrhosis,PBC），1型糖尿病（type 1 diabetes,T1D），神经系统受累的重症肌无力（myasthenia gravis，MG），攻击肾小球足细胞的特发性膜性肾病（membranous nephropathy，IMN）以及由B细胞和T细胞介导的甲状腺功能亢进。其特点是免疫反应，以位于某一器官内的自身抗原为目标时，参与慢性炎症性疾病的发展的自身免疫过程，具有器官特异性。第二种类型是系统性AD，如免疫网络失衡的银屑病（psoriasis），系统性红斑狼疮（systemic lupus erythematosus,SLE）等，涉及多个组织与器官，可能是自身抗原的系统分布所致。

系统性红斑狼疮的靶向药物治疗

SLE是一种特异性，慢性，损害性的自身免疫性疾病。一般涉及肾脏，心和脑等许多脏器。主要症状有皮肤红斑、关节疼痛、容易疲倦和肾功能退化等。
世界范围内SLE发病人群主要为育龄期妇女，患者中女性是男性的10倍,
在我国SLE年发病人数大约在100万人以上，并呈逐年上升趋势。

随着对SLE发病机制的逐渐深入，与靶向治疗的兴起，SLE的治疗方案也曾出不穷。

SLE的靶向药物治疗主要分为 以细胞因子，B细胞，T细胞，激酶（Janus kinase，JAK）以及布鲁顿酪氨酸激酶 (Bruton's tyrosine kinase，BTK)5个靶点的靶向治疗。

这里我们将介绍以B细胞激活因子（BAFF，是B淋巴细胞发育成成熟血浆B细胞所必需。）为靶点的药物——贝利木单抗（belimumab），是作用于B细胞激活因子的单克隆抗体，贝利木单抗已经通过FAD的使用批准，可以用于治疗SIE成人患者。并且在2019年获取中国国家药品监督管理局的批准并上市。是全球首个获得批准运用于治疗SLE的生物制剂。

当免疫系统产生有害的Ig1-X抗体，攻击人体自身的组织时，贝利木单抗会通过减少B细胞活动从而发挥作用。贝利木单抗会与血清中可溶性BAFF结合，阻止其与受体结合，从而抑制B细胞增殖及分化为产生抗体的浆细胞，使得自身免疫性B细胞凋亡，从而减少血清中自身抗体，达到治疗的目的。

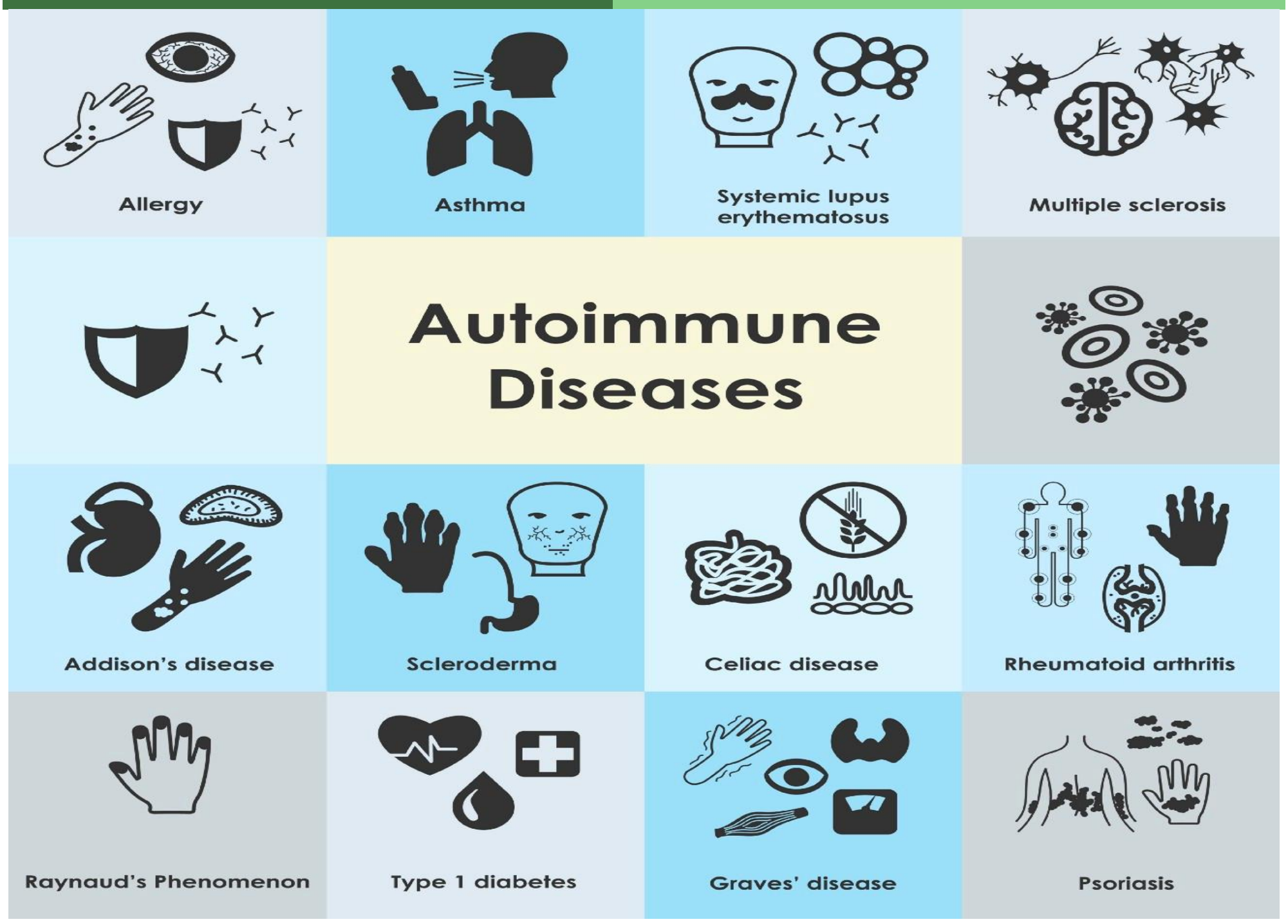
贝利木单抗这是一种长期的治疗方法，可能需要六个月的时间。

自身免疫性贫血

自身免疫性贫血是一组疾病，特点是免疫系统功能障碍，导致生成会把红细胞当成体内异物攻击的自身抗体。自身免疫性溶血性贫血是一组少见疾病，可以发生于任何年龄。女性多于男性。其中半数自身免疫性溶血性贫血的原因不详（特发性自身免疫性溶血性贫血）。自身免疫性溶血性贫血可由其他疾病引起或与其他疾病伴发，例如系统性红斑狼疮（狼疮）或淋巴瘤，自身免疫性溶血性贫血也可归因于青霉素等某些药物的使用。

溃疡性结肠炎的谜题

在2020年的八月份，日本首相安倍晋三宣布由于溃疡性结肠炎的复发，他辞去首相职务。据报道安倍晋三从十几岁就患有溃疡性结肠炎，可见其病理漫长。反复发作，并且无法痊愈。溃疡性结肠炎（Ulcerative Colitis）是一种局限于结肠粘膜及粘膜下层的炎症过程。溃疡性结肠炎的病因至今仍不明。虽有多种学说，但目前还没有肯定的结论。一些专家认为溃疡性结肠炎是一种自身免疫性疾病，他们认为，免疫系统将结肠中有助于消化的 "友好细菌 "误认为是有害的感染，导致结肠和直肠发炎。遗传基因也会影响是溃疡性结肠炎发展。如果家族中有结肠炎的患者，那么其他人的发病率将大大提高。例如调查表明非白人患者比白人患者约少50%。



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