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The Relative Deficiency of Potassium Ions in Nerve Cells Causes Abnormal Functions and Neurological and Mental Diseases

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ABSTRACT

The difference of intracellular potassium (K^+) and extracellular sodium (Na^+) concentrations in nerve cells plays an important role in the functional activities of the nervous system. The maintenance of this difference mainly depends on the number and efficiency of Na, K-ATPase. However, due to the functional activity of nerve cells, this system often loses its balance. An undetectable phenomenon is the relative deficiency of potassium in nerve cells in specific brain regions or neural network structures, which leads to dysfunction of specific nerve cell populations or brain regions, thus leading to different types of neurological disorders or diseases. The relative deficiency of potassium ions in nerve cells may be caused by the competitive failure of nerve cells to effectively use potassium ions stored in the body, and the core reason may be related to insufficient potassium obtained through diet or effectively absorbed by the digestive system. Therefore, a simple strategy is to treat a patient by taking appropriate potassium orally. This paper presents a case with great success by using such a method to treat a patient with major depression.

1. INTRODUCTION

The nervous system is divided into central nervous system and peripheral nervous system. Neural tissue mainly consists of neurons and glial cells. Neurons are the basic unit to form network, transmit neural information and realize basic neural regulation and higher cognitive functions. A basic feature of neurons is excitability, which is mainly determined by intracellular potassium ion (K^+) and extracellular sodium ion (Na^+) [1-8]. Potassium ion is involved in the formation of membrane potential of nerve cells, which is commonly known as membrane resting potential. The membrane potential exists in both neurons and glial cells, but more attention is often paid to the resting potential of neurons. The membrane potential am-

plitude of mammalian neurons is determined by the concentration difference established by high intracellular (approximately 140 mM) and low extracellular concentrations of potassium ions (approximately 5 mM) [9]. Such a difference not only determines the level of membrane potential, but also has an important influence on the excitability of neural cells, that is the propagation of neuronal action potential. Therefore, maintaining the concentration difference of potassium ions inside and outside cells is quite important for nerve cells to perform different functions. Additionally, the difference in sodium ions between the intracellular (5 - 15 mM) and extracellular (approximately 145 mM) concentrations of nerve cells determines the strength of the bioelectric activities (action potentials) of these nerve cells [9]. Therefore, such a K^+/Na^+ system in nerve cells plays a key role in neural functions related to their electrical activity.

Under normal conditions, the electrical activity of nerve cells is completed by the coordinated excitation of group cells, which is a group network (neural circuit) rather than an individual behavior [10]. The activity of a network group of nerve cells also reflects the function of the neural network or a functional association with several specific brain regions [11]. The membrane potential level of each neuron that is connected to other neurons in a neural network is different; however, as long as the average level of neuronal population in a specific circuit or brain region reaches a basic value, the normal activity of the neural network can be maintained. Such electrophysiological characteristics do not need special attention for most neuroscientists because even if they are engaged in scientific research, they only observe some or a certain kind of neurons and could achieve the goal of research and observation. In fact, we also know that if a certain number of nerve cells in a certain brain region are randomly detected, such detections can be completed *in vitro* or *in vivo* with intracellular recording by inserting glass microelectrode or flexible nanopipettes inside of nerve cell or using patch clamp technology [12-18]. As a result, it could be found that the membrane potential value of each neuron varies greatly, and some are higher, reaching more than −90 mV (the neuron membrane potential is internally negative and externally positive), some are relatively smaller (several millivolts), but on average it can maintain a relatively normal range in a group of neurons. This is the same as the heart rate of normal people in a quiet state. Some people are faster, and some people are slower, but a group of population has a normal range.

2. THE FUNCTIONS AND DYNAMIC STABILITY MECHANISM OF INTRACELLULAR POTASSIUM ION IN NERVE CELLS

Individual differences in membrane potentials of different nerve cells have not attracted the attention of researchers to think deeply, that is, it should be taken for granted. Even for neuroscientist, if it has nothing to do with their research, it is not worth paying attention to. But if we seriously consider and answer the following questions, so what is the situation?

1) Why do different neurons have different membrane potentials?

2) Within what range can the average level of the membrane potential of a group of neurons in the brain region or function related neural network predict normal, otherwise it is abnormal?

3) What impact will such a change have if it goes beyond a certain range?

So far, neuroscience research has paid little attention to these issues, because the study of the structure and function of genes and molecules and their relationship with behavior has attracted more interest from peers. Another reason is that researchers believe that this is not a cutting-edge scientific problem because neuroscience has a very clear understanding of the basic principles of nerve cell membrane potential [1-18]. There is no more scientific problem worthy of in-depth attention and construction that sounds very interesting. It has been demonstrated by many studies that the establishment of high concentration of potassium ions in cells, including nerve cells, is mainly completed by Na, K-ATPase on the cell membrane [19-29]. This enzyme can work all the time under the condition of obtaining ATP energy supply, pumping extracellular potassium ions into the cells, and maintaining the high concentration of potassium ions in the cells within a certain range. This activity mechanism starts from embryonic cells developing into nerve cells until nerve cell death, just like the sun we see from the earth, it rises from the east and sets from the west, providing light energy to all things on the earth day by day, but none really cares.

As long as our brain works normally, we have every reason to believe that Na, K-ATPase has been functioning to support the function of each nerve cell. Neuroscientists examine the function of the brain just as an economist cares about a country's GDP. Appropriate growth is an important indicator of sound economic development, and the average GDP of a country is a measure of whether the country is at the level of developed, medium, or non-developed countries.

3. RELATIVE DEFICIENCY OF POTASSIUM IONS IN NERVE CELLS RELATED TO THE FUNCTIONAL CHANGES AND NEUROLOGICAL DISEASES

The same is true for our brain. People believe that as long as we maintain a good mental state, it has nothing to do with the important role of Na, K-ATPase. A person is tired, takes a rest, and once he/she recovers to a good mental activity state, it means normal. He/she does not know until a certain period that his/her nervous system and mental state have problems, and then he/she realizes that there is a certain problem with his body. Why is this so? Because human beings have not fundamentally recognized that in order to regulate the function of the body, our brain always emerges a relative deficiency of potassium ions in nerve cells in the process of information exchange with the external environment and mental activities of adaptation. Once such a relative deficiency exceeds a certain degree, and cannot be effectively recovered, then will cause neurological and mental diseases. How to understand such a process?

The relative deficiency of potassium ion is first reflected in different individual neurons, which is related to the degree of functional activity. If the neurons in a brain region or neural network cannot get reasonable rest in the process of group activities, then the potassium ions in their cells will slowly decrease, which can explain why different nerve cells show different levels of membrane potential. If the whole brain is highly active that is what we usually call stress activity, then most neurons will lead to the reduction of potassium in cells, resulting in the relative deficiency of potassium ions in neurons in most brain regions, which may lead to neuropsychiatric diseases such as depression. If there is a relative deficiency of potassium ions in some or specific brain regions or neural functional circuits, other mental diseases may occur such as Alzheimer's disease (AD) and Parkson's disease (PD).

The research on these neuropsychiatric diseases has always attracted great attention from scientific and social circles, and scientific exchanges and conferences are also emerging one after another. Scientists have done a lot of research work and put forward many exciting hypotheses and theories. Drug companies have also made endless scientific research and development investment in these bright assumptions and theories, developing drugs and treatments, hoping to solve the difficulties faced by mankind. But so far, it is true that there is often a glimmer of dawn in different corners of science, but in the end, these glimmers of dawn have been eclipsed and the sunny sky cannot be seen.

The main reason for the relative deficiency of intracellular potassium ions may be related to the characteristics of nerve cells in specific brain regions or neural circuits, especially the strength and efficiency of the mechanism of establishing the concentration gradient of intracellular potassium ions. Some neurons have strong functions, that is, the activity of Na, K-ATPase is strong, and enough potassium ions can be obtained from the outside of the cell. The source of the potassium ions in the extracellular fluid in nervous system is mainly supported through the blood circulation, and part of which is the transfer of intracellular potassium ions to the extracellular fluid (cerebrospinal fluid) during neural activity.

Only from the perspective of the nervous system alone, the deficiency of potassium in a brain region can lead to the decline of the average level of membrane potential, and then affect the network function between nerve cells. If the deficiency of potassium in nerve cells exists for a long time, it can cause the structural and functional abnormalities of this kind of specific nerve cells, and this is because of that potassium ions not only play an important role in maintaining the membrane potential, but also participate in a variety of functions involved in gene expression and regulation, and metabolism, etc. [30-34].

The relative deficiency of potassium ions existing in a functional neural circuit, a neural cell population in a specific brain region with the same function, and even whole brain may be due to two reasons. On the one hand, it is related to the amount and activity of Na, K-ATPase in nerve cells. The activity of

Na, K-ATPase is a process of bioenergy (ATP) consumption and molecular energy conversion, but a speculation based on non-experimental evidence may also be related to cosmic energy [35]; on the other hand, it is related to potassium content in intake diet or food, and the capability of digestive tract absorption as well as the conditions of potassium storage and distribution in organs, tissues and cells, which is explained in details in another paper [36]. For the nervous system, a reason that needs to be emphasized in particular for the relative deficiency of potassium may be related to the deficiency of potassium ions allocated by the body through the brain blood circulation, but the root is the deficiency of potassium obtained through the digestive system, which may be caused by the insufficient potassium in intake diet and /or the insufficient absorption of potassium ions by the digestive system. Such a relative deficiency is easy to confuse our judgment because it is relative and could result in different abnormal functional manifestations in different organs and tissues including nervous system. The differential development of organs and tissues may also play an important role because the overall utilization of potassium in the body is a dynamic and competitive process, and the nervous system usually has a competitive advantage. Such a competitive advantage may lead to the relative deficiency of potassium and functional changes in non-neural organs, tissues and cells early, while the nervous system may show the symptoms of relative potassium deficiency later. However, if some individual nervous systems have no obvious competitive advantage compared with the other organs and tissues, the relative deficiency of potassium in the body may also appear first in the nervous system, especially the change or overall reduction of cerebral blood flow can lead to the relative deficiency of potassium in the brain, triggering different types of functional changes and neurological diseases. For example, the depressive disorder may result in long-term stress together with the relative deficiency of potassium in the whole brain; PD patients may be mainly caused by the relative deficiency of potassium in dopaminergic neurons in the first place; the early stage of AD patients may be related to the relative deficiency of potassium in the hippocampus, but the late stage presents the overall brain deficiency of potassium. Similar mechanisms from different aspects can give explanations for other functional abnormalities of the nervous system and neurological disorders or diseases. Therefore, this may be a common and key mechanism for the different functional changes or diseases in the nervous system.

Of course, the relative deficiency of sodium ions in body also affects the functions of the nervous system due to the overemphasis on the importance of low salt diet, which may be a disaster of the so-called "medical health knowledge" dissemination, particularly in the developed countries, however, the body's monitoring of extracellular sodium ions and the use of edible salt are often easier to correct the relative deficiency of sodium ions.

4. TREATMENT STRATEGY FOR THE RELATIVE DEFICIENCY OF POTASSIUM IONS IN NERVE CELLS

Therefore, the treatment means should first start from providing potassium to supply the deficiency of potassium in the body through intake diet or drugs. A case reported here, the treatment of a depressed patient with sustained-release KCl tablets resulted in a much unexpected good result, and the patient recovered completely after about one month's treatment, providing direct and key evidence for the ideas proposed in this paper.

5. CASE REPORT: A DEPRESSION PATIENT TREATMENT

The patient in this report is a 28-year-old female. The patient admitted that he had mainly experienced repeated attacks of anxiety and depression to varying degrees in the past year or so, and was tested by professional medical institutions for anxiety and depression psychological evaluation in April 2022, indicating that he had reached the scoring standard of mild anxiety and severe depression. She has experienced a lot of discomfort in all aspects of life, including being very upset and bored with the subway management work she has always loved and worked for more than seven years, and applying for resignation on the grounds of health. However, based on her good work performance over the past years, the company's management staff promised her to take a paid leave for a period of time before making a final

decision. She asked me for advice on her physical condition and possible treatment. Based on my clinical medical background, research experience in depression and current research progress in the treatment of depression, especially the theoretical framework described in this article, I propose that she try the treatment of non-depression conventional drugs (similar to diet therapy) to increase the intake of potassium ions. On the premise of not using any other drug treatment, she was recommended for oral administration of 0.5 G KCI sustained-release tablets three times a day after daily diet, a total of 1.5 g/day. After a week of treatment, she felt that her anxiety and depression declined, and she significantly improved in the following two weeks. After about four weeks of treatment, her anxiety and serious depression behavior basically disappeared. She then told the company to withdraw her resignation report and returned to her original job after about five weeks of leave for treatment. I suggested she continue to take KCl sustained-release tablets irregularly and appropriately, and adjust living and diet habits at the same time, especially taking foods with high potassium content reasonably and appropriately, including some meat foods. After further follow-up, she is completely recovered. Therefore, I believe that this is a typical episode of acute anxiety and depression caused highly possibly by changing her eating habits in the past period, especially during the COVID-19 epidemic in China over the past two years when she did not get enough potassium ions in daily diets, which may also be the key reason for the onset of most young patients with depression.

6. CONCLUSION AND SIGNIFICANCE

The functional abnormalities and pathogenesis of neurological and neuropsychiatric diseases are proposed to be due to the relative deficiency of potassium in the special nerve cells, brain regions and circuits in the nervous system, which is related to the competitive utilization of potassium ion and utilization efficiency in different organs and tissues of the body. The root reason may be that the body could not get enough potassium through daily intake diet. Therefore, the basic strategies for treating the functional abnormalities and neurological and neuropsychiatric diseases are to correct the relative deficiency of potassium ions in the nerve cells.

In addition, the relative deficiency of potassium in relation to the dysfunctions and diseases of non-neural tissues is discussed in other papers.

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CONFLICTS OF INTEREST

The author declares no conflicts of interest regarding the publication of this paper.

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