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Research Progress of Copper Metabolism and Disease Occurrence in Brain

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Abstract: Copper is one of the indispensable metal elements in the human body. It participates in the regulation of metabolism and enzyme synthesis in the physical, and maintains the progress and evolution of the body and life activities. Especially in the nervous system, copper is also participated in myelination E, regulating synaptic plasticity activity likewise excitatory neuron Death and the signal cascade. The human brain is the controller of all life activities, so it is necessary to maintain the homeostasis of copper metabolism in the brain. Research shows that steady state copper metabolism disorders plays a crucial part in Alzheimer's disease (AD), Parkinson's disease (PD), and neurodegenerative diseases such as Wilson disease (WD). It is involved in the etiopathogenesis of many neurodegenerative diseases.Consequently, regulating this process is expected to furnish a fresh orientation for the study of the etiology of this disease. This article reviews the research progress on the correlation between the imbalance of copper metabolism homeostasis and the occurrence of diseases, so as to provide evidence for subsequent research.

1. Introduction

Copper is the second requisite microelement in people's body. It is an important component of copper ferment and related proteins in the body. It exists in almost all life forms and plays an extremely important role in body activities[1]. It is involved in a variety of physiological pathways[2], therefore, the state and content of copper need to be strictly controlled. Especially in the brain, copper is involved in neurotransmitter synthesis and oxidation biological processes such as breathing. Which has a important role in a variety of neurological functions,Copper plays an indispensable role in cell function, and its metabolic disorder or imbalance often leads to serious and irreversible cell damage, leading to the occurrence of diseases. Both copper excess[3] and copper deficiency[4] are closely related to human diseases, and excess copper can lead to neuronal damage[5]. Copper also has neurotoxic effects, and excess copper can lead to the development of certain neurological diseases. Copper not only has REDOX activity, but also plays a casting in regulating cell signaling and plasticity. The concentration of copper in the brain is second only to that in the liver. The transport of copper through CTR1 and ATP7A to different brain regions across

the blood-brain barrier is another important metabolic pathway. Other studies have reported that copper content is different in different brain regions, with higher copper concentration in CA1 region of hippocampus, amygdala, cerebellum and diencephalon[6].

Copper mainly combines with proteins in the brain, exists in the form of macromolecular complexes. Excessive copper can cause toxicity through the generation of superactive hydroxyl radicals, and then destroy the nearby macromolecules[7]. In the body, copper transporters can regulate copper content. CTR1 and DMT1 are transmembrane transporters that can transport extracellular copper ions to the cell body, while ATP7A located in the Golgi apparatus can transport copper from the Golgi reticulum to the cell . Copper can also from CTR1 and ATP7A transporters in cells through the endothelium and vein to accumulate in the brain[8-9],by participating in the electron transfer function of oxidases and REDOX reactions[10]. Studies have shown that cuprase has catalytic agility, energic tailorism, immuno function, prevention of ROS injury and transmission of neurons in the body[6]. It is further shown that copper has an irreplaceable casting in the systema nervosum peripheric um.

2. Diseases Associated with Abnormal Copper Metabolism

The brain is made up of neurons, which have different functions, as an example for controlling body movements, processing signals and responding accordingly. However, neurons in the brain cannot be regenerated, so that the damage of these neurons is irreversible and even leads to the dysfunction of the body[11-12].

Neurodegenerative diseases are most common in Settings where copper metabolism in the brain is dysregulated. Neurodegenerative disease is a kind of progressive degenerative disease, which can cause the loss or even death of neuronal structure or function in the brain, and promote the body into a disease state, and then lead to functional disability. Neurodegenerative diseases include many diseases. Many scholars have studied on the cause of neurodegenerative diseases, found that oxidative stress, oxidative damage, inflammation, etc., because of inflammation in the aetiopathogenesis of Molecular Neurodegeneration pathema the casting of widely agreed to be[13-14] in recent years, many studies have shown that copper metabolism disorders are involved in neurodegenerative pathema, particularly alzheimer's and Parkinson's pathema.

2.1 Copper and Alzheimer's Disorder

Alzheimer's disease (AD) is a neurodegenerative pathema with insidious development. It is mainly clinically manifested as dementia, for instance decreased learning memory, anterograde amnesia, cognitive impairment, and behavioral changes. Deposition of insoluble amyloid-β (Aβ) peptide and neurofibrillary tangles is the most critical neuropathological feature of Alzheimer's disease. Pathological protein deposits, including Aβ peptide and hyperphosphorylated Tau, have also been considered as the “cause” of Alzheimer's pathema[15]. Amyloid protein and metal Cu2+ act together, leading to the accumulation of extracellular copper ions, damage neurons and nerve cells, and eventually lead to inflammatory reaction[16]. Chen et al. used proteomics method to find that excessive copper can interfere with the brain function of mice and aggravate the neurodegenerative changes in the mouse model of Alzheimer's disease[17]. The findings suggest that the buildup of copper in the brain can worsen Alzheimer's pathema in people with the disease. In addition, studies have shown that copper ion also has REDOX activity, and its accumulation in neurons will cause oxidative stress, resulting in neuronal cell death through the generation of comparative oxidative products[18].

2.2 Copper and Parkinson's Disease

Parkinson's disease (PD) is a hackney neurodegenerative pathema in middle-aged and senium people. Parkinsonism pathema,the second modal neurodegenerative disorder, is peculiarity by the forfeit of dopamine-producing neurons, resulting in cell bodies in the dense substantia nigra, and the accumulation of misfolded α-synuclein and additional substances, known as Lewy bodies. The clinical symptoms of PD patients are static tremor, bradykinesia, myotonia, abnormal posture and gait, until the loss of self-care ability[19]. Studies have shown that the morbidity of Parkinson's pathema is higher in copper exposure environment. AshokK, SheetalG, PraveenS[20] et al. used proteomics to conduct bioinformatics analysis of copper and spade metabolic proteins in neurodegenerative pathemas and found that the pathogenic mechanism was related to secreted acidic proteins and cysteine-rich proteins. Copper entered cells through copper transporters attached to the cell membrane. Two regions of α-synuclein have been identified as copper binding sites with high affinity, which is of great biological significance for the research of the etiopathogenesis of Parkinson's pathema.

2.3 Copper and Wilson's Disease

Wilson's pathema (Wilson's pathema) is an autosomal instealth genetic pathema of copper supersession. The main pathological feature is ATP7B gene mutation. ATP7B is the core mutant gene of copper metabolism disorder in the etiopathogenesis of Wilson's pathema. It locates in 13q14.3 and contains 20 introns and 21 exons, which is responsible for encoding P-type copper transport ATPase. However, ATP7B membrane protein has eight transmembrane structures, and its core structure includes: the N-terminal copper ion-binding domain has six subunit methylated CpG binding domains, eight transmembrane domains, ATP nucleotide binding domains, and a C-terminal[21]. The major active sites of ATP7B protein were mainly studied in the 6 MBD subunits. Each MBD can bind one copper ion, among which MBD1-4 mainly plays a role in the regulation of copper catalytic activity, while MBD5 and MBD6 are the main pragmatic subunits that determine the efficiency of copper transport[21-22]. The etiology of Wilson's disease is mainly a disease induced by the homeostasis of copper metabolism in the body environment, but some studies have confirmed that there is a correlation between the severity of copper deposition in the brain tissue[23-24]. In the brain, copper toxicity is first buffered by astrocytes, leading to increased levels of copper in brain tissue and changes in the brain microenvironment leading to subsequent damage to neurons and other glial cells. Different brain regions show different neurological symptoms with different severity of lesions.

3. Copper and Other Diseases

In addition to the above cases, such as amyotrophic lateral sclerosis (ALS), is a kind of belong to fatal neurodegenerative diseases is also included in the conditions of imbalance of copper within the steady state in the cerebrum. ② Menkesdisease: an X-linked implicit genetic pathema bought about ATP7A gene mutations contribute to copper assimilate disorder, characterized by neurodevelopmental delay and seizures. ③ Hereditary CP deficiency (aceruloplas-minemia) is an autosomal implicit genetic disease bought about CP gene salation, which is also a neurodegenerative pathema associated with abnormal copper metabolism. Aceruloplas-minemia is characterized by neurological symptoms and small cell anemia related to systemic iron accumulation, usually accompanied by decreased serum copper concentration.

4. Conclusion

As the population ages, the number of person inflicted neurodegenerative pathemas such as Alzheimer's and Parkinson's is increasing year by year. Although the etiopathogenesis of neurodegenerative pathemas has been thoroughly explored by many scholars, it still needs a long process to be fully elucidated. The casting of inflammation in neurodegenerative pathema has been recognized and emulated. This provides us with a new perspective in the foreclosure and therapy of neurodegenerative pathemas and exists important guiding significance.

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