Journal of Clinical and Nursing Research, 2025, Volume 9, Issue 2
http://ojs.bbwpublisher.com/index.php/JCNR
Online ISSN: 2208-3693
Print ISSN: 2208-3685

The Role of Central Inflammation in Postoperative Cognitive Dysfunction

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Abstract: Postoperative cognitive dysfunction is a typical complication, which can be referred to as POCD. This complication is common in elderly patients. Among them, POCD is mainly manifested in the function of patients with attention deficit and memory reduction after surgery, among which serious patients are prone to personality change, which affects their social behavior ability. In the context of the current era, the cause of POCD is not clear, combined with the results of most studies, it is found that central nervous inflammation, is a key factor affecting POCD. From the perspective of central inflammation, this paper analyzes the relationship between central inflammation and POCD, and discusses the mechanism of action, aiming at effectively preventing and treating POCD and providing a reference for subsequent research in related fields.

Keywords: Central inflammation; Postoperative cognitive dysfunction; Effects

Online publication: March 6, 2025

1. Introduction

In 1955, Bedford found that patients with postoperative cognitive dysfunction occurred, until 1998 Moller of this phenomenon, namely the postoperative cognitive dysfunction (POCD). POCD patients mainly manifested mental disorders and social ability decline, and even some serious patients lost the ability to take care of themselves, and the postoperative recovery effect was poor. Previous studies have found that POCD usually appears after major surgery, such as coronary artery bypass, and has a high postoperative incidence. However, the pathogenesis of POCD has not been clarified, and the incidence of POCD is higher in the postoperative group of elderly patients. According to recent research results, there is a close relationship between inflammation induced by the use of narcotic drugs and POCD. Based on this, the role of central inflammation in POCD is discussed.

2. Central inflammation and postoperative cognitive dysfunction

2.1. Central inflammatory response

In the human body, the central nervous system (CNS) can accept all kinds of information, integrate and process the information, transmit the coordinated movement output, or store it well to facilitate the human body to carry out learning and memory [1]. The central nervous system is one of the special parts of the human immune system. If it is not subjected to inflammation and injury, the circulating immune cells contained in the human body cannot penetrate the central nervous system through the blood-brain barrier. Under normal circumstances, the human body does not contain special antigen-transfer cells. The central nervous system of the human body, containing microglia, T cells, etc., can secrete many cytokines after activation, deepening the neuroinflammatory response of patients after surgery. The emergence of neuroinflammation, easily leads to the emergence of neurodegenerative diseases in the human body, in which inflammatory mediators can effectively play a role in the central nervous system in the following ways:

(1) Cytokines such as interleukin, can penetrate into the area around the ventricle, or through the form of transport, effectively break through the blood-brain barrier [2].

(2) Human cytokines and BBB endothelial cell receptors fusion, easy to affect the central nervous system, and then secrete a large number of inflammatory factors.

(3) In the human CNS, when the vagus nerve and afferent nerve are affected by surrounding immune factors, they are easy to activate the central inflammatory pathway. The microglia of the central nervous system can effectively recognize signals and transmit them through stimulant mediators, which have an effect on astrocytes and bring about a more serious second reaction.

2.2. Central inflammation and POCD

The key influencing factors of POCD after surgery include neuroinflammation, microglial cell activation, etc. Central inflammation is usually indirectly caused by glial cell activity, so inflammation can be appropriately regulated by regulating glial cell activity [3]. In the composition of human nerve cells, microglia and astrocytes are usually included, and astrocytes occupy the majority and play an important role, while microglia belong to the immune cells of the central nervous system, and their lineage is similar to that of surrounding macrophages. Through the activation of microglia, many cytokines can be produced, and then a large number of inflammatory factors appear in the field of the central nervous system, such as TNF-α, IL-6, etc. Through the excessive release of pro-inflammatory factors, the phosphorylation of tau protein can be accelerated, and amyloid protein accumulation can be caused [4]. In addition, if the microglia in the human body are over-activated, the release of neurotoxins will increase significantly, thus changing the mode of neurotransmitter transmission and affecting the plasticity of synapses, resulting in postoperative cognitive dysfunction. The excessive activation of microglia in the hippocampus of the brain leads to high levels of IL-1 and inflammatory mediators, which will destroy learning and memory. Older brains, with an increase in microglia, exhibit inflammatory features, synaptic plasticity, and cognitive deficits [5]. With the increase of human age, the activation of microglia is easy to causes the intensification of the role of stressors, which further affects central nervous inflammation and has adverse effects on the cognitive function of the human body.

Through the clinical trial activities carried out on the animal model and the analysis of the test data, it is not difficult to find that there is a relationship between the activation of the immune system and the cognitive ability of the animals after the operation, and the operation is easy to cause hippocampal-dependent memory impairment

and promote the increase of plasma cytokines [6]. Some medical studies have found that the lipopolysaccharides (LPS) in mice can induce the brain of mice, resulting in an increase in microglia in the brain, cell morphology will also change, showing obvious activation form, bringing more serious neuroinflammatory response. Among them, the out-of-control phenomenon of inflammation will cause cognitive decline in mice, and then bring a series of complications. Neuroinflammation induced by microglia activation caused by surgical trauma is accompanied by cognitive dysfunction, and the pro-inflammatory factors in glia are dependent, which can easily induce hippocampal inflammation [7]. Studies have shown that surgical injury can easily lead to hippocampal-dependent cognitive impairment. There is a correlation between hippocampal interleukin and cognitive function in the brain of mice, that is, increased expression of interleukin and decreased cognitive function. IL-6 can activate NF-κB signal, causing neuroinflammation in elderly mice, and thus forming postoperative cognitive dysfunction. Some clinical studies have shown a link between peripheral inflammatory markers and POCD, including an association between inflammatory cytokines and neurocognitive decline in patients undergoing surgery [8]. Hudetz found that postoperative peripheral serum IL-6 was closely associated with elevated CRP levels. After the above research and discussion, it can be found that surgery can activate the homeostasis response, effectively release inflammatory mediators, cause an inflammatory cascade reaction, and finally cause POCD.

3. The possible mechanism of central inflammation in postoperative cognitive dysfunction

Through research activities, Kiecolt-Glaser found that in animal and clinical experiments, postoperative cognitive dysfunction is closely related to central nervous inflammation, in which the expression of inflammatory factors is up-regulated and the release is increased, such as IL-1β, IL-6 and so on. Due to the excessive release of pro-inflammatory factors, the tau protein phosphorylation problem is brought about, resulting in excessive activation of microglia [9]. Among them, the play of neurotoxic substances can bring about the transformation of neurotransmitter transmission, affect the plasticity of synapses, and then lead to postoperative cognitive dysfunction in patients. At the same time, there is a decrease in anti-inflammatory substances in the body, which causes inflammatory factors in the brain, leading to cognitive impairment [10]. This study focuses on the activation of microglia and analyzes the role of central inflammation in POCD.

In the central system of the human body, microglia are mononuclear phagocytes, which belong to the first line of defense of the human brain. They can play a neuroprotective role, make the brain free from the influence of external factors, effectively reduce the damage caused by pathogens, clean up the cell debris, truly protect the stability of the human brain, and play a leading role in the inflammatory response. Microglia can be divided into two forms, which are resting and activated. Under normal conditions, microglia are in a resting state, and only after being stimulated by exogenous antigens, they will be rapidly activated, gradually form small cells, slender branch pseudopodia appearance transformation, forming amoeba shape, effectively play its phagocytic role, and eliminate the possible existence of neurotoxins in the human body, cell debris, which results in better protection [11]. In this regard, in the course of specific experiments, the average volume of microglia can be understood according to the overall volume, and the activated number of microglia can be effectively judged. According to the previous literature, taking mice as experimental objects, it can be found that the operation tends to cause a significant increase in microglia activation in young mice within a week after the operation, and it is easy to bring about inflammation in the hippocampus, resulting in a decrease in the cognitive function of the mice. After a week, all

indexes of the mice gradually returned to normal, according to the experimental results. It can be concluded that the operation brought about the activation of microglia, and then caused the decline of cognitive function in mice [12]. Through the study of elderly mice, it was found that aging will promote the increase of microglia activation, and its characteristics have a high similarity with chronic degenerative diseases. Combined with the condition of healthy old mice, the activation of microglia appeared in the body, which mainly showed a significant increase in MHC-ii. From the perspective of the surgical model of elderly mice, the activation of microglia in the hippocampus is usually maintained for more than two weeks, and the increase in the activation ratio leads to the reduction of memory in mice [13]. Based on this, it is reasonable to infer that microglia activity is the key factor causing POCD problems. According to the results of the study, it can be found that the emergence of peripheral inflammation, will affect the central nervous system, from the human level, the path of activation of microglia includes the following:

(1) The human internal and external neuroinflammation will release a large number of inflammatory factors, and then stimulate the liver, and with the vagus nerve transmission, bring serious inflammation;

(2) Increased permeability of the blood and cerebrospinal fluid barriers in the human body can transmit peripheral inflammatory factors into the central nervous system [14];

(3) In the internal and external inflammatory factors of the human body, they can play the role of the barrier carrier of blood and cerebrospinal fluid, and use their dependence to achieve protein transport and smooth integration into the central nervous system;

(4) The blood circulation in the human body will bring inflammatory factors to bind to the barrier of blood and cerebrospinal fluid, fuse endothelial cells, and make immune molecules enter the brain [15].

Under the pathway, which cannot be found, the human central system's neuroimmunity is usually transmitted by the vagus nerve. Under the third path, the brain in the human body contains an increase in inflammatory factors, the main reason refers to peripheral circulation stimulation, easy to drive behavior change. But no matter what path, the result is the inflammatory response of the central nervous system, and the activation of microglia can release inflammatory factors and strengthen the connection with the brain, leading to neurodegenerative diseases in patients.

4. Conclusion

To sum up, in the context of the current era, although the mechanism of action of POCD has not been clearly defined, experimental studies by many scholars have proposed that central inflammation is the main cause of POCD. Starting from the pathogenesis of POCD, the key influence of central inflammation cannot be found. In this regard, a series of measures should be taken to inhibit central inflammation in the human body. Continuously improve the medical effect, to avoid affecting the postoperative cognitive ability of patients. In the current medical field, a series of studies have been carried out on POCD, but the exact mechanism has not been clarified, so it is necessary to carry out in-depth research. By carrying out a series of treatments of central inflammation, good results can be achieved, and the prevention and treatment of POCD can be explored, providing reference for the follow-up to find appropriate treatment methods, and effectively reducing the incidence of POCD.

Funding

Jiangsu University Student Innovation and Entrepreneurship Project, "Study on the Mechanism of TLR4-mediated Central Inflammation Induced by Glial Cell Activation to POCD" (Project No.: 202313980027Y)

Disclosure statement

The authors declare no conflict of interest.

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