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Research Progress in the Pathogenesis of Post-stroke Depression

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Abstract: Post-stroke depression is an affective disorder that occurs after stroke. Its pathogenesis has not yet been fully understood, and it mainly involves neurobiology, neuroanatomy, and psychology. This paper provides an overview on the neurobiological mechanism of post-stroke depression to further understand post-stroke depression and to provide references for further research.

Keywords: Post-stroke depression; Neurotransmitter; Neuroanatomy; euroimmunity; Cytokines; Neuroplasticity

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Post-stroke depression (PSD) refers to the incidence of diseases with main symptoms such as abnormal mood, loss of interest, and anxiety etc. under the influence of various factors after a stroke. Studies have shown that the incidence of post-stroke depression is about 33%, therefore, PSD imposes certain burdens on the patients, families and society[1]. Currently, there are mainly two viewpoints on PSD, namely the reactive mechanism and the primary endogenous mechanism. This paper mainly elaborates from the aspects of neurotransmitter, neuroanatomy, and neuroimmunity etc.

1 Neurotransmitter theory

The central neurotransmitter is involved in mental and emotional activities. Currently, the neurotransmitter theory has become one of the PSD pathogenesis generally accepted by most scholars. In the central nervous system, 5-hydroxytryptophan (5-HT) and norepinephrine(NE) are important neurotransmitters that are involved in regulating mental activity and emotional response. When a stroke affects the neurotransmitter pathway, it will further damage the emotional center of the brain, reduce the content of 5-HT and NE, and further lead to depression. Li Xia et al. found that the establishment of a brain stroke model resulted in damage to hippocampus and cortical neurons, leading to decreased transmitter and synthesis functions, and PSD[2]. Robinson believes that focal ischemia may lead to the reduction of monoamine neurotransmitters in the frontal and temporal lobes and the basal ganglia, which is related to depression, especially 5-HT, NE and dopamine (DA)[3].

2 Neuroanatomy

PSD is also closely related to the lesion sites of the stroke. Shi Yu et al. believe that lesions in different areas of the brain will not only cause symptoms of neurological deficits in the corresponding functional areas, but will also lead to PSD, which is one of the important factors for post-stroke patients to develop depression[4]. The frontal lobe of the brain plays a certain role in regulating emotion and consciousness. Robinson found that the incidence and progress of PSD is closely related to the brain lesions, especially the frontal pole, which is associated with the highest incidence in addition to the frontal lobe, left basal ganglia, and temporal lobe etc[3]. Lincoln et al. showed that the left hemisphere of the brain is more likely to cause depression than the brainstem and right hemisphere, and the closer the lesions are to the frontal pole and the base, the higher the incidence[5]. In addition, the amygdala and hippocampus are

related to cognition and emotion. Chen Yu et al.carried out MRI observations and found that the bilateral hippocampus and amygdala in patients with PSD decreased in volume, and demonstrated the possible mechanism of PSD from the aspects of imaging[6]. Studies have also found that patients with cerebral ischemia lesions in the frontal lobe are more likely to suffer from PSD than lesions in other parts of the brain[7].

3 Neuroimmunity

In recent years, there have been more and more researches on the correlation between PSD with hypothalamic-pituitary-thyroid axis (HPT axis) and hypothalamic-pituitary-adrenal axis (HPA axis). Inhibition of the HPT axis after cerebral ischemia reduces the level of serum free triiodothyronine, which may be the reason for the aggravation of depressive symptoms in PSD patients; on the other hand, stroke can lead to the activation of the HPA axis and increases the release of adrenal cortex hormones and glucose corticosteroids, producing a negative feedback effect in the hippocampus, which leads to the incidence of PSD[8]. Ma Ying et al. believe that cytokines, as important neurotransmitters in the neuroimmune system, may play an important role in the pathogenesis of depression[9]. Studies have found that the production of IL-1β, IL-2, and TNF-α in the serum of PSD patients is increased[10]. These inflammatory factors activate the HPA axis to cause excessive release of cortisol, thereby aggravating the patients' depressive symptoms. After drug intervention, the level of cytokines can be reduced, thereby inhibiting the HPA axis and alleviating the symptoms of depression[11].

4 Cytokine hypothesis

Spalletta et al. believe that the incidence of PSD may be related to pro-inflammatory cytokines[12]. After having stroke, the production of pro-inflammatory cytokines such as IL-1β, INF-α, and IL-18 is increased, further resulting in the exhaustion of neurotransmitters such as 5-HT etc. in the peripheral area of the brain, which will lead to PSD. Pascoe et al. believe that ischemic inflammation may be one of the causes of PSD[13]. Anti-inflammatory and antidepressant treatment can alleviate depression-like behaviors. In addition, after studying the relationship between these inflammatory markers and PSD, it may be of certain significance to the development of clinical biomarkers.

5 Neuroplasticity hypothesis

The hippocampus plays a certain role in the regulation of human emotions, and also plays a vital role in the growth, differentiation and plasticity of neurons. Rupshi et al. believe that adverse stress can affect the proliferation of hippocampal cells, which may be of great significance for understanding the damage of hippocampal structure and functions in psychotic patients[14]. Similarly, in animal stress models, atrophy and loss of neurons and glial cells in the hippocampus and prefrontal cortex were observed[15]. In addition, Liu Cong et al.found that changes in the function or expression of various synapse-related proteins may be the mechanism of depression[16]. After antidepressant treatment, the depressive behavior of PSD model rats was significantly altered, and the plasticity of hippocampal neurons was further improved[17]. Some scholars used Chinese medicine to intervene in PSD model rats, which was found to enhance the plasticity of hippocampal neurons, thereby alleviating depression symptoms[18-20].

6 Conclusion

In summary, through the above elaborations on the mechanisms of PSD, the author found that the pathogenesis of PSD is closely related to many factors, including neurotransmitters, neuroanatomy, neuroimmunity, and neuroplasticity, etc. In addition, there are Brain-gut Axis theory, genetic epilogy, and mental psychology, etc. These factors are interrelated and influence each other, which together lead to the incidence and progress of PSD. Therefore, studying the inter-correlations between multiple mechanisms of PSD may have some significance for the in-depth study of PSD.

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