Neurodegenerative disease refers to a class of diseases that cause dysfunction of the nervous system due to the death of nerve cells. These diseases are caused by the gradual death of neurons, which has a serious impact on the lives of patients. Therefore, the treatment and prevention of neurodegenerative diseases is one of the focuses of modern medical research. Microenvironment refers to the chemical composition and physical properties of the microenvironment around nerve cells, which can enable the growth and function of nerve cells [1].

The microenvironment affects the activity and life activity of nerve cells by influencing a series of parameters such as pH, oxygen concentration and temperature of the surrounding environment. For neurodegenerative diseases, the microenvironment can delay the death and damage of nerve cells by improving the environment at the lesion site. Microenvironment intervention is mainly used in the research and treatment of neurodegenerative diseases, which can play a role in protecting nerve cells by changing a series of parameters such as oxygen, temperature and pH value of the surrounding environment. The ability of nerve cells to repair themselves is stimulated by improving the environment of the diseased site [2].

Neurodegenerative diseases are caused by the death of nerve cells, and the environment around nerve cells has a direct effect. Therefore, by changing the chemical composition and physical properties of the surrounding environment of nerve cells, the death and damage of neurons can be delayed. Microenvironment regulation is mainly used in the protection and repair of neurons, and plays an important role in the treatment of neurodegenerative diseases [3]. Studies have found that by regulating the environment around nerve cells, the self-repair ability of nerve cells can be stimulated to prevent a large number of nerve cells from dying, thereby improving the quality of life of patients [4]. In conclusion, the study of microenvironment brings new ideas for the treatment and prevention of neurodegenerative diseases. The electrolyte balance of the neuron microenvironment is the basis for maintaining the normal excitability of neurons [5]. The microenvironment of the nervous system is inseparable from the interaction of many types of cells. Astrocytes are the main type of glial cells in the central nervous system (CNS) and are important regulators of brain function. Astrocytes maintain synaptic homeostasis through a variety of physiological functions, including uptake and recovery of neurotransmitters, provision of energy substances, synthesis of lipids, the release of glial transmitters, maintenance of extracellular potassium levels, and water balance. In neurodegenerative diseases, these physiological functions change as neurodegeneration progresses [6]. The transformation of resting astrocytes into reactive astrocytes in the pathological microenvironment is a common feature of many neurodegenerative diseases. But it is now recognized that astrocytes are heterogeneous and that differences in this microenvironment also have an impact on the progression of neurodegenerative diseases. In addition, calcium signaling in astrocytes is related to its various physiological functions and its interaction with synapses. Disturbance of astrocyte calcium signaling has detrimental effects on neural microenvironment and synaptic function and is involved in disease development [6].

Microlgia in the central nervous system also plays an important role in the immune system and in regulating neuronal homeostasis. The activated form of microlgia protects the central nervous system from neuronal damage caused by inflammation. Microlgia induce a neuroinflammatory cascade by releasing reactive oxygen species, active nitrogen, and cytokines to change the microenvironment. In addition, microlgia play a role in the central monitoring of the microenvironment and can adjust according to the dynamic characteristics of the neuronal microenvironment to maintain the steady-state function of the microenvironment [7]. Therefore, the differentiated state of microlgia is most likely caused by the different neuronal microenvironments.

In recent years, extracellular vesicles called exosomes have emerged, which play an important role in information exchange between cells under physiological and pathological conditions. These vesicles (30-150 nm) contain proteins, RNA, and lipids, and bystander cells induce vesicles to internalize, leading to functional abnormalities. In neurodegenerative diseases, pathological proteins are strongly associated with age-related autophagy and lysosomal dysfunction, which leads to their stable presence in specific secretory vesicles, thereby influencing disease progression through the microenvironment [8]. In addition, injecting secretory vesicles isolated from neurodegenerative patients into the hippocampus of wild-type mice was neurotoxic in vivo, leading to increased tau phosphorylation [9]. Therefore, secretory vesicles packed with pathogenic molecular patterns may play an important role in neuroaging phenotypic transmission.

For accurate assessment and diagnosis of age-related neurodegeneration, vesicles secreted in various body fluids may be the best biomarker, which further clarifies the importance of the microenvironment for neurodegenerative diseases. Using blood-brain barrier (BBB) permeability to secretory vesicles, brain-derived exosomes can be detected in the peripheral circulation [10]. Neuron-secreting vesicles in serum showed elevated levels of phosphorylated tau-181 and 231, Aβ-42, and insulin receptor substrate 1 in the AD group. In PD, in addition to alpha-synuclein detected in the CSF, many non-coding Rnas are significantly upregulated in secretory vesicles, including miR-153 and miR-409-3p. Therefore, the precise detection of secretory vesicles and other microenvironments contributes to the in-depth understanding of the disease mechanism, so as to effectively intervene in the process of neurodegenerative diseases.

The microenvironment of neurodegenerative diseases is complicated, which is not only related to single pathological factors. In patients with neurodegenerative diseases, a large number of glial cell proliferation and activated small colloidal cells and other immune inflammatory reactions can be seen near the aging plaques [1].

Therefore, the impact on the microenvironment may be the result of a combination of factors. In the pathogenesis of neurodegenerative diseases, the precise influence of the microenvironment and whether it contributes to the formation of functional neural circuits are important questions in cell replacement therapy strategies, and further investigation of the operational mechanisms of the pathological microenvironment is required. The current research focuses on the effects of simplified individual pathogenetic factors and the entire pathogenetic environment on disease. APP, PS-1, and Aβ can only partially simulate the pathogenesis. Future research should explore the influence of pathological factors of neurodegenerative diseases on the microenvironment from both in vitro and in vivo, so as to promote the strategy of cytoplasmic replacement therapy.
References


Competing interests
The authors declare no conflicts of interest.

Authors contributions
Yuxue Jiao and Yang Yang conceptualized and wrote the manuscript. Yang Yang reviewed and modified the manuscript. All authors approved the final version of the manuscript.

Acknowledgments
This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Citation

Executive editor: Qian-Nan Xie.
Received: 25 June 2023, Accepted: 25 June 2023, Available online: 25 June 2023.
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