The pericyte: an important cell type for central nervous system diseases

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Pericytes are contractile cells that wrap around the endothelial cells of capillaries throughout the body. They play an important role in regulating the blood brain barrier (BBB) and blood spinal cord barrier (BSCB). Our research group is committed to finding out the characteristics of pericytes, which directly impact pathophysiological processes in CNSD. We recently reported that the pericytes from brain microvascular and spinal cord microvascular possessed the distinguishable abilities of tube-formation and migration, which provide a better understanding of pericytes in CNS. The awareness of regional microvascular pericytes heterogeneity in CNS obliges consideration that brain and spinal cord microvascular networks might differ in their barrier properties or other capacities. In vivo, our research indicated that pericytes might promote angiogenesis in spinal cord injury C57BL/6 mice. Melatonin ameliorated the loss of blood vessels and disruption of BSCB to exert a protective effect on SCI, which might be mediated by increased pericyte coverage. The upregulation of angiopoietin-1 in pericytes could inhibit inflammation and apoptosis to protect the microvessels. Generally speaking, melatonin could stabilize microvascular barrier function and microcirculation of SCI, whose mechanism was to promote the repair of the damaged BSCB.

Keywords: pericytes; blood brain barrier; blood spinal cord barrier; central nervous system diseases; microvascular

Central nervous system diseases mainly contain brain diseases and spinal cord diseases. These diseases are mostly related with the disruption of blood brain barrier (BBB) and blood spinal cord barrier (BSCB). BBB disruption may contribute to the development of brain-related diseases, such as Alzheimer, and stroke [1, 2]. The most extensive studies about BSCB disruption are traumatic spinal cord injury (SCI). Endothelial cells, pericytes, astrocytes and microglia make up the functional BBB and BSCB. Pericytes, surrounding the microvessels are involved the proliferation, migration and differentiation of ECs [3]. There are several structural and functional differences between the BBB and BSCB. Some data highlighted that the barrier function of spinal cord microvascular ECs in BSCB expressed less amount of tight junction proteins ZO-1 and occludin, adherence junction protein VE-cadherin, β-catenin and transporter molecules P-glycoprotein than that in the BBB [4]. Our reports showed remarkable differences between brain microvessel pericytes (BMPs) and SCMPs (SCMPs) [5, 6]. BMPs had enhanced tubeformation ability compared with SCMPs. The migration ability of SCMPs was increased compared with that of BMPs. The distinguishable abilities of tubeformation and migration between BMPs and SCMPs, which might be mediated by VEGF, connexin 43, N-cadherin and desmin, provide a better understanding of pericytes in CNS. The awareness of regional microvascular network might differ in their barrier...
properties or other capacities. The constructed in vitro BBB model had the basic characteristics of BBB in vivo in morphology, structure and barrier function\[^7\]. BSCB capillary permeability may be heightened by regional reductions of pericytes at cellular basis\[^8\].

The previous studies about SCI ignored the reaction within the spinal cord, while they mostly focused on how to improve sensory motor function. The micro-environment of spinal cord will be altered by any alterations. Reduction of the BSCB breakdown will result in marked neuroprotection\[^9, 10\]. The spinal cord microcirculation is critically important for maintaining the normal function of spinal cord neurons, glial cells, and axons\[^11\]. The former works of our research group focus on the pericytes and BSCB in the process of SCI pathology. Pericyte coverage was significantly reduced, and the expression of angiopoietin-1 and Bcl-2 was inhibited, while the expression of intercellular cell adhesion molecular-1 and Bax was improved after SCI\[^12\]. Pharmaceuticals can have a considerable influence on microcirculation\[^13\]. In our study, melatonin, as a directly free radicals scavenger, was detected its ability of improving circulation and restoring BSCB. Melatonin significantly reduced BSCB permeability, restrained microvessel loss, attenuated edema, protected the tight junction proteins, endothelial cells, and pericytes, decreased the number of cell apoptosis, and reduced MMP3/AQP4/HIF-1/VEGF/VEGFR2 expression after SCI. In one word, our results clearly demonstrated that melatonin could stabilize microvascular barrier function and microcirculation of SCI, whose mechanism was to promote the repair of the damaged BSCB\[^14\].

In the field of CNS pericyte biology, excellent recent progress has led to a greater promotion of their functional importance in health and disease\[^15\]. We have begun to uncover the different characteristics of pericytes from the CNS microvascular, which influence neuronal function. The researches about the neurovascular model of neurological diseases have begun to alter the way we now think about neurodegeneration. Nowadays, it is relatively little that we know about the role of pericytes in major human brain diseases, such as stroke, Alzheimer’s disease, Parkinson’s disease and et al. Future studies should be more concentrated on the close relationship between pericytes and other cell types and the pharmaceuticals developing to treat the CNS diseases.

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References


