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Increased miR-21-3p in injured brain microvascular endothelial cells following traumatic brain injury aggravates blood-brain barrier damage by promoting inflammation and apoptosis through targeting *MAT2B*

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Our previous researches have reported that increased miR-21-5p in brain following traumatic brain injury (TBI) could improve the neurological outcome through alleviating blood-brain barrier (BBB) damage. miR-21-3p is another mature miRNA derived from pre-miR-21 after dicer procession other than miR-21-5p. Its roles in various diseases, such as tumors and myocardial disease aroused great interest for research in recent years. To further explore the function and underlying mechanism of miR-21, especially miR-21-3p in regulating the pathological development of BBB damage after TBI, we recently focused on studying the impact of miR-21-3p on apoptosis and inflammation in brain microvascular endothelial cells (BMVECs), the major cellular component of BBB. We performed controlled cortical impact on mouse brain, and employed the oxygen glucose deprivation/reoxygenation (OGD)-treated bEnd.3 cells injury model. We found that miR-21-3p level in BMVECs from injured cerebral cortex of controlled cortical impact (CCI) mice, and bEnd.3 cells with OGD treatment were both increased after injury. For *in vitro* experiments, downregulation on miR-21-3p level by transfecting miR-21-3p antagomir in cultured cells alleviated OGD-induced BBB damage, characterized by decreased BBB leakage and increased expression of tight junction proteins. Besides, miR-21-3p antagomir could control inflammatory response by inhibiting the activity of NF-κB signaling, and suppress cell death by anti-apoptosis. Using luciferase reporter assay and a *MAT2B*-silenced shRNA vector, we further proved that miR-21-3p exerted above functions through targeting *MAT2B*. In addition, *in vivo* experiments also confirmed that intracerebroventricular infusion of miR-21-3p antagomir could alleviate BBB leakage after TBI. It reduced Evans blue extravasation and promoted the expression of tight junction proteins, thus contributed to improve the neurological outcome of CCI mice. Taken together, increased miR-21-3p in BMVECs after TBI was bad for restoration of injured BBB. Downregulation on miR-21-3p level in injured brain could be a promising therapeutic strategy for BBB damage after TBI.

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