The Alteration of the Blood-Brain Barrier Integity in POCD Induced by Orthopedic Surgery and the Relative Mechanisms

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Background: The underlying causes of postoperative cognitive decline (POCD) in old patients remained elucidated, and there were little descriptions on mechanisms associated with the blood-brain barrier (BBB) disruption during POCD. Since tight junctions and adhision junctions play important roles in the integrity of the BBB which can be influenced by matrix metalloproteinase-9 (MMP-9) and vascular endothelial growth factor A (VEGFA) , our study aims to investigate the effect of orthopedic surgery on the blood-brain barrier integrity and spacial working memory in aged rats as well as the regulation of MMP-9 and VEGFA in this process.

Methods: 234 male wistar rats, 18-20 months, 500-600 g, were randomly divided into 3 groups with 78 rats in each group (group C), propofol group (group P) and propofol plus surgery group (group PS). Animals in group P were treated with propofol 0.7mg•kg^{-1}•min^{-1} for 20 minutes through tail vein, while rats in group PS experienced orthopedic surgery with propofol anesthesia (0.7mg•kg^{-1}•min^{-1} for 20 min). At day 1,3,7 after experiments, we assessed their spacial working memory via Y maze (n=8). We detected their hippocampal BBB permeability with Evans blue qualification (n=6). Alteration of tight junction claudin-3, claudin-5, ZO-1 and adhision junction VE-cadherin were measured by western blot (n=6). Finally we assessed MMP-9 nd VEGFA via immunohistochemistry staining (n=6).

Results: Compared with group C, the ability of recognition memory of rats in group PS to novel environment was poor in the Y maze test at day 1, 3 and 7. Compared with group C, rats in group PS has higher Evans blue quantification at day 1 and day 3. Additionally, tight junctions claudin-3, ZO-1 and adhision junction VE-cadherin were found down-regulated at day 1 and 3, with MMP-9 positive cells in CA1 area and VEGFA positive cells in DG area significantly increasing at day 1. Animals in group P were not found significant difference of recognition memory or BBB component compared with group C.

Conclusion: Orthopedic surgery disrupts the BBB integrity via down-regulation of tight junctions claudin-3 and ZO-1 as well as adhision junction VE-cadherin,

leading to impaired spatial working memory in aged rats, and the up-regulation of MMP-9 and VEGFA were involved in this process.