TRPV4 instigate endothelial disruption and secondary damage in spinal cord injury

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Abstract

The role of Transient receptor potential vanilloid type 4 (TRPV4) is not recognised in the pathology of spinal cord injury (SCI). Herein we studied the expression and the role of TRPV4 in the pathology of endothelial dysfunction and secondary damage after SCI. TRPV4 expression was increased during the inflammatory phase after SCI, and followed injury-dependent expression pattern. Intracellular Ca^{2+} at similar time points as determined using two-photon microscopy exhibit bi-phasic increase after SCI. TRPV4 activation using specific agonist rendered the organization of endothelial cells, affected the tight junction expression in hCMEC/D3 BBB cell line *in vitro* and increase the glial components in the spinal cord. Pharmacological suppression of TRPV4 using specific antagonist or in Trpv4 knockout mouse preserved endothelial cells, attenuated the inflammatory cytokines and chemokines, promotes vascular stabilization, prevented the tight junctions protein degradation, and blood-spinal cord barrier (BSCB) break down after SCI. Likewise, Trpv4 knockout mouse abridged secondary damage and improved behavioral outcomes after SCI. Thus, our result suggests that increased TRPV4 expression was associated with the disrupted organization of endothelial cells, early inflammatory phase of SCI, tissue damage, vascular destabilization, BSCB breakdown, and cell injury. TRPV4 inhibition serves as a promising therapeutic strategy to attenuate neuropathic pain, secondary damage and promoting vascular stabilization after SCI.

Keywords: - TRPV4; Spinal Cord Injury; Endothelial cells Vascular stabilization; Inflammation; Functional Recovery; Blood-spinal cord barrier