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Hydrogen-Rich Saline Activated Autophagy via HIF-1 α Pathways in Neuropathic Pain Model

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Abstract

Background: Neuropathic pain is a chronic and intractable pain, with very few effective analgesics. It involves an impaired cell autophagy process. Hydrogen-rich saline (HRS) reportedly reduces allodynia and hyperalgesia in a neuropathic pain model; however, it is unknown whether these effects involve autophagy induction.

Methods: We investigated the relationship between HRS and cell autophagy in a neuropathic pain model generated by chronic constriction injury (CCI) in Sprague-Dawley rats. Rats received an intraperitoneal injection of HRS (10 mL/kg daily, from 1 day before until 14 days after CCI), 3MA (autophagy inhibitor), 2ME2 (HIF-1α inhibitor), or EDHB (HIF-1α agonist). The mechanical withdrawal threshold (MWT) and thermal withdrawal latency (TWL) were tested 1 day before and 1, 3, 7, 10, and 14 days after the operation. HIF-1α and cell autophagy markers in the spinal cord were evaluated by western blotting and real-time PCR assays at 14 days after CCI. Autophagosomes with double membranes were identified by transmission electron microscopy.

Results: CCI caused behavioral hypersensitivity to mechanical and thermal stimulation in the hind-paw of the injured side. HRS improved MWT and TWL, activated autophagy, and increased autophagosomes and autolysosomes in CCI rats. 3-MA aggravated hyperalgesia and allodynia and suppressed autophagy, while EDHB attenuated hyperalgesia and activated the autophagy procedure and the HIF-1α downstream target gene BNIP3. HIF-1α inhibitors reversed the regulatory effects of HRS on autophagy in CCI rats at 14 days after spinal cord injury.

Conclusion: HRS reduced mechanical hyperalgesia and activation of cell autophagy in neuropathic pain through a HIF1-dependent pathway.

Figures

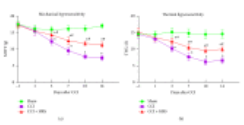

Figure 1 *Effect of HRS on thermal...*

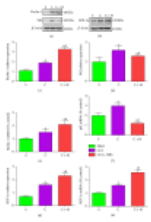

Figure 2 *The expression of autophagy associated...*

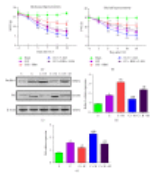

Figure 3 *Effect of 3-MA on thermal...*

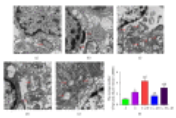

Figure 4 *Autophagosomes (Aps) and autolysosomes (Als)...*

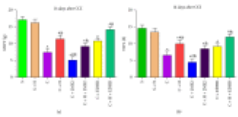

Figure 5 *Effect of EDHB and HRS...*

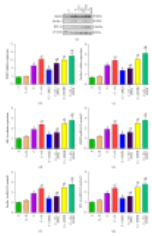

Figure 6 *The expression of BNIP3, Beclin-1,...*

All figures (7)

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Nucleotide (RefSeq)
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