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Pain Medicine

Characterization of Macrophage/Microglial Activation and Effect of Photobiomodulation in the Spared Nerve Injury Model of Neuropathic Pain

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Objective: Neuropathic pain is common and debilitating with limited effective treatments. Macrophage/microglial activation along ascending somatosensory pathways following peripheral nerve injury facilitates neuropathic pain. However, polarization of macrophages/microglia in neuropathic pain is not well understood. Photobiomodulation treatment has been used to decrease neuropathic pain, has anti-inflammatory effects in spinal injury and wound healing models, and modulates microglial polarization in vitro. Our aim was to characterize macrophage/microglia response after peripheral nerve injury and modulate the response with photobiomodulation.

Methods: Adult male Sprague-Dawley rats were randomly assigned to sham (N = 13), spared nerve injury (N = 13), or injury + photobiomodulation treatment groups (N = 7). Mechanical hypersensitivity was assessed with electronic von Frey. Photobiomodulation (980 nm) was applied to affected hind paw (output power 1 W, 20 s, 41 cm above skin, power density 43.25 mW/cm^2, dose 20 J), dorsal root ganglia (output power 4.5 W, 19 s, in skin contact, power density 43.25 mW/cm^2, dose 85.5 J), and spinal cord regions (output power 1.5 W, 19 s, in skin contact, power density 43.25 mW/cm^2, dose 28.5 J) every other day from day 7-30 post-operatively. Immunohistochemistry characterized macrophage/microglial activation.

Results: Injured groups demonstrated mechanical hypersensitivity 1-30 days post-operatively. Photobiomodulation-treated animals began to recover after two treatments; at day 26, mechanical sensitivity reached baseline. Peripheral nerve injury caused region-specific macrophages/microglia activation along spinothalamic and dorsal-column medial lemniscus pathways. A pro-inflammatory microglial marker was expressed in the spinal cord of injured rats compared to photobiomodulation-treated and sham group. Photobiomodulation-treated dorsal root ganglion macrophages expressed anti-inflammatory markers.

Conclusion: Photobiomodulation effectively reduced mechanical hypersensitivity, potentially through modulating macrophage/microglial activation to an anti-inflammatory phenotype.

Key words: Inflammation; Macrophage; Microglia; Neuropathic Pain; Photobiomodulation; Spared Nerve Injury