The Mechanistic Basis for Photobiomodulation Therapy of Neuropathic Pain by Near Infrared Laser Light

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Background and Objective: Various irradiances have been reported to be beneficial for the treatment of neuropathic pain with near infrared light. However, the mechanistic basis for the beneficial outcomes may vary based on the level of irradiance or fluence rate used. Using in vivo and in vitro experimental models, this study determined the mechanistic basis of photobiomodulation therapy (PBMT) for the treatment of neuropathic pain using a high irradiance.

Study Design/Materials and Methods: In vitro experiments: Cultured, rat DRG were randomly assigned to control or laser treatment (LT) groups with different irradiation times (2, 5, 30, 60, or 120 seconds). The laser parameters were: output power¼960mW, irradiance ¼300mW/cm2, 808nm wavelength, and spot size¼3cm diameter/area¼7.07cm2, with different fluences according to irradiation times. Mitochondrial metabolic activity was measured with the MTS assay. The DRG neurons were immunostained using a primary antibody to b-Tubulin III. In vivo experiments: spared nerve injury surgery (SNI), an animal model of persistent peripheral neuropathic pain, was used. The injured rats were randomly divided into three groups (n¼5). (i) Control: SNI without LT; (ii) Short term: SNI with LT on day 7 and euthanized on day 7; (iii) Long term: SNI with LT on day 7 and euthanized on day 22. An 808nm wavelength laser was used for all treatment groups. Treatment was performed once on day 7 postsurgery. The transcutaneous treatment parameters were: output power: 10 W, fluence rate: 270mW/cm2, treatment time: 120 seconds. The laser probe was moved along the course of the sciatic/sural nerve during the treatment. Within 1 hour of irradiation, behavior tests were performed to assess its immediate effect on sensory allodynia and hyperalgesia caused by SNI.

Results: In vitro experiments: Mitochondrial metabolism was significantly lower compared to controls for all LT groups. Varicosities and undulations formed in neurites of DRG neurons with a cell body diameter 30 mm or less. In neurites of DRG neurons with a cell body diameter of greater than 30 mm, varicosities formed only in the 120 seconds group. In vivo experiments: For heat hyperalgesia, there was a statistically significant reduction in sensitivity to the heat stimulus compared to the measurements done on day 7 prior to LT. A decrease in the sensitivity to the heat stimulus was found in the LT groups compared to the control group on days 15 and 21. For cold allodynia and mechanical hyperalgesia, a significant decrease in sensitivity to cold and pin prick was found within 1 hour after LT. Sensitivity to these stimuli returned to the control levels after 5 days post-LT. No significant difference was found in mechanical allodynia between control and LT groups for all time points examined.

Conclusion: These in vitro and in vivo studies indicate that treatment with an irradiance/fluence rate at 270mW/cm2 or higher at the level of the nerve can rapidly block pain transmission. A combination therapy is proposed to treat neuropathic pain with initial high irradiance/fluence rates for fast pain relief, followed by low irradiance/fluence rates for prolonged pain relief by altering chronic inflammation. Lasers Surg. Med. 49:516–524, 2017._ 2017 Wiley Periodicals, Inc.