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Light Promotes Regeneration and Functional Recovery and Alters the Immune Response After Spinal Cord Injury†

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Background and Objectives: Photobiomodulation (PBM) has been proposed as a potential therapy for spinal cord injury (SCI). We aimed to demonstrate that 810 nm light can penetrate deep into the body and promote neuronal regeneration and functional recovery.

Study Design/Materials and Methods: Adult rats underwent a T9 dorsal hemisection, followed by treatment with an 810 nm, 150 mW diode laser (dosage = 1,589 J/cm^2). Axonal regeneration and functional recovery were assessed using single and double label tract tracing and various locomotor tasks. The immune response within the spinal cord was also assessed.

Results: PBM, with 6% power penetration to the spinal cord depth, significantly increased axonal number and distance of regrowth ($P < 0.001$). PBM also returned aspects of function to baseline levels and significantly suppressed immune cell activation and cytokine/chemokine expression.

Conclusion: Our results demonstrate that light, delivered transcutaneously, improves recovery after injury and suggests that light will be a useful treatment for human SCI. Lasers Surg. Med. 36:171–185, 2005.

Key words: astrocytes; corticospinal tract; footprint analysis; low power laser irradiation; macrophage; microglia; photobiomodulation; rat; retrograde and anterograde tract tracing

INTRODUCTION

Damaged central nervous system axons fail to regenerate following spinal cord injury (SCI) in adult mammals. Despite vigorous research, including use of anti-inflammatory drugs [1], X-irradiation [2,3], elimination of inhibitory factors in the spinal cord [4–9], provision of neurotrophic factors [10–14], and cell transplantation [15–22], there currently is no cure for the sensory or motor deficits seen following injury. After SCI, a secondary injury occurs that is mediated in part by the immune response [23] and magnifies the impairment [23–25].

Photobiomodulation (PBM), also known as light therapy, low power laser irradiation, or low level laser irradiation, is an effective treatment for cutaneous wounds and promoting peripheral nerve regeneration [26–29]. This modulation in recovery is attributed to a light absorption mechanism [30] rather than through the production of heat [29,31,32]. Research has shown that dosages of 0.001–10 J/cm^2 stimulate cellular activity (such as DNA, RNA, and protein production, proliferation, and motility) while dosages greater than 10 J/cm^2 inhibit activity [33].

Following SCI, high dosage PBM in combination with transplantation resulted in an increase in axonal sprouting, decreased scar formation, and improved weight bearing and step taking in dogs and rats in comparison to transplantation alone [34–36]. These studies indicate that PBM may have a number of therapeutic effects following SCI, potentially by decreasing the inflammatory response at the spinal cord lesion site.

Invasion/activation of immune cells has been under investigation as a potential mediator of secondary injury [23]. A variety of cell types invade or are activated within the first hours to days after SCI, including neutrophils, macrophages, microglia, astrocytes, and T and B lymphocytes [25,37–46]. These cells are primarily activated or drawn into the lesion area by pro-inflammatory cytokines and chemokines, expressed within the first few hours after injury [42,47–49]. Recent evidence suggests that alteration of cell invasion/activation after SCI improves functional recovery. Research demonstrated that depletion of macrophages improved locomotion, spared white matter, preserved myelinated axons, supported axonal sprouting and reduced cavitation [50]. Anti-inflammatory drugs also increased tissue sparing [51] and promoted functional recovery [21,52].

To date, no study has assessed the axonal regrowth of specific tracts or the recovery of specific locomotor functions

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