Light therapy alters gene expression after acute spinal cord injury

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Secondary injury in the spinal cord, which results in axonal degeneration, scar and cavity formation and cell death, occurs around the site of the initial trauma and is a primary cause for the lack of axonal regeneration observed after spinal cord injury (SCI). The immune response after SCI is under investigation as a potential mediator of secondary injury. Treatment of SCI with 810 nm light suppresses the immune response and improves axonal regeneration.

We hypothesize that these beneficial effects observed in the injured spinal cord are accompanied by alterations in gene expression within the spinal cord, particularly of those genes involved in secondary injury and the immune response. To test this hypothesis, a dorsal hemisection at vertebral level T9 was performed. The injured spinal cord from rat was then exposed to laser light (810nm, 150mW, 2,997 seconds, 0.3cm² spot area, 1,589 J/cm²) and spinal cord samples, including the injury site, were harvested at 6 and 48 hours and 4 days post-injury. Total RNA was extracted and purified from the lesioned spinal cord and cDNA copies were either labeled with [32P] for microarray analysis or amplified and analyzed with a polymerase chain reaction (PCR).

Microarray results revealed a suppression of genes involved in the immune response and excitotoxic cell death at 6 hours post-injury, as well as cell proliferation and scar formation at 48 hours post-injury in the light treated group. Analysis of the PCR products revealed that light treatment resulted in a significant suppression of expression of genes that normally peak between 6 and 24 hours post-injury, including the pro-inflammatory cytokine interleukin 6 (IL6), the chemokine monocyte chemoattractant protein 1 (MCP-1) and inducible nitric oxide synthase (iNOS; p<0.05). Genes expressed earlier than 6 hours post-injury, such as IL1b, tumor necrosis factor a (TNFa) and macrophage inflammatory protein 1a (MIP-1a) were not affected by light treatment.

Although the precise role some of these genes play in axonal regeneration after spinal cord injury is currently unclear, these data demonstrate that light therapy has an anti-inflammatory effect on the injured spinal cord, and may reduce secondary injury, thus providing a possible mechanism by which light therapy may result in axonal regeneration.
**Temporary suppression of clonus in humans by brief photostimulation.**

Brain Res. 1985 Aug 5;340(1):109-13

**Walker JB.**

In this double-blind study, 21 subjects with spastic paraparesis due to chronic spinal cord injury received irradiation to the skin overlying the radial, median and saphenous nerves with a helium-neon laser (632.5 nm, 1 mW, 20 Hz) or sham treatment. Subjects in the experimental group demonstrated complete clonus suppression after 40 s of irradiation, an effect identical to that observed previously after peripheral electrical nerve stimulation. Subjects who received placebo did not demonstrate this phenomenon. Because such laser irradiation produces no detectable thermal effect, the results indicate that photochemical reactions initiated by laser may trigger neural activity.

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**Transplantation of embryonal spinal cord nerve cells cultured on biodegradable microcarriers followed by low power laser irradiation for the treatment of traumatic paraplegia in rats**


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OBJECTIVE: This pilot study examined the effects of composite implants of cultured embryonal nerve cells and laser irradiation on the regeneration and repair of the completely transected spinal cord. STUDY METHODS: Embryonal spinal cord nerve cells dissociated from rat fetuses and cultured on biodegradable microcarriers and embedded in hyaluronic acid were implanted in the completely transected spinal cords of 24 adult rats. For 14 consecutive post-operative days, 15 rats underwent low power laser
irradiation (780 nm, 250 mW), 30 min daily. Assessment included somatosensory evoked potential (SSEP) recordings, tissue microscopy, and functional recovery assessment.

RESULTS: Eleven of the 15 (73%) showed different degrees of active leg movements and gait performance, compared to 4 (44%) of the 9 rats with implantation alone. In a control group of seven rats with spinal cord transection and no transplantation or laser, six (86%) remained completely paralyzed. Three months after transection, implantation and laser irradiation, SSEPs were elicited in 69% of rats (p = 0.0237) compared to 37.5% in the nonirradiated group. The control group had no SSEPs response. Intensive axonal sprouting occurred in the group with implantation and laser. In the control group, the transected area contained proliferating fibroblasts and blood capillaries only.

CONCLUSIONS: This suggests: 1.) These in-vitro composite implants are a regenerative and reparative source for reconstructing the transected spinal cord. 2.) Post-operative low power laser irradiation enhances axonal sprouting and spinal cord repair.

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