Parkinson’s Disease/NIR Light Research Papers:

**Therapeutic effect of near infrared (NIR) light on Parkinson’s disease models.**

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**Source:** Department of Neurology, Medical College of Wisconsin

**Abstract:**

Parkinson’s disease (PD) is a neurodegenerative disorder that affects large numbers of people, particularly those of a more advanced age. Mitochondrial dysfunction plays a central role in PD, especially in the electron transport chain. This mitochondrial role allows the use of inhibitors of complex I and IV in PD models, and enhancers of complex IV activity, such as NIR light, to be used as possible therapy. PD models fall into two main categories; cell cultures and animal models. In cell cultures, primary neurons, mutant neuroblastoma cells, and cell cybrids have been studied in conjunction with NIR light. Primary neurons show protection or recovery of function and morphology by NIR light after toxic insult. Neuroblastoma cells, with a gene for mutant alpha-synuclein, show similar results. Cell cybrids, containing mtDNA from PD patients, show restoration of mitochondrial transport and complex I and IV assembly. Animal models include toxin-insulted mice, and alpha-synuclein transgenic mice. Functional recovery of the animals, chemical and histological evidence, and delayed disease progression show the potential of NIR light in treating Parkinson’s disease.


**Neuroprotection of midbrain dopaminergic cells in MPTP-treated mice after near-infrared light treatment.**

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**Abstract:**

This study explores whether near-infrared (NIR) light treatment neuroprotects dopaminergic cells in the substantia nigra pars compacta (SNC) and the zona incerta-hypothalamus (ZI-Hyp) from degeneration in 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)-treated mice. BALB/c albino mice were divided into four groups: 1) Saline, 2) Saline-NIR, 3) MPTP, 4) MPTP-NIR. The injections were intraperitoneal and they were followed immediately by NIR light treatment (or not). Two doses of MPTP, mild (50 mg/kg) and strong (100 mg/kg), were used. Mice were perfused transcardially with aldehyde fixative 6 days after their MPTP treatment. Brains were processed for tyrosine hydroxylase (TH) immunohistochemistry. The number of TH(+) cells was estimated using the optical fractionator method. Our major finding was that in the SNC there were significantly more dopaminergic cells in the MPTP-NIR group compared to the MPTP group (35%-45%). By contrast, in the ZI-Hyp there was no significant difference in the numbers of cells in these two groups. In addition, our results indicated that survival in the two regions after MPTP insult was dose-dependent. In the stronger MPTP regime, the magnitude of loss was similar in the two regions.
(approximately 60%), while in the milder regime cell loss was greater in the SNc (45%) than ZI-Hyp (approximately 30%). In summary, our results indicate that NIR light treatment offers neuroprotection against MPTP toxicity for dopaminergic cells in the SNc, but not in the ZI-Hyp.


Reduced axonal transport in Parkinson’s disease cybrid neurites is restored by light therapy.

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ABSTRACT: BACKGROUND: It has been hypothesized that reduced axonal transport contributes to the degeneration of neuronal processes in Parkinson’s disease (PD). Mitochondria supply the adenosine triphosphate (ATP) needed to support axonal transport and contribute to many other cellular functions essential for the survival of neuronal cells. Furthermore, mitochondria in PD tissues are metabolically and functionally compromised. To address this hypothesis, we measured the velocity of mitochondrial movement in human transmitochondrial cybrid “cytoplasmic hybrid” neuronal cells bearing mitochondrial DNA from patients with sporadic PD and disease-free age-matched volunteer controls (CNT). The absorption of low level, near-infrared laser light by components of the mitochondrial electron transport chain (mtETC) enhances mitochondrial metabolism, stimulates oxidative phosphorylation and improves redox capacity. PD and CNT cybrid neuronal cells were exposed to near-infrared laser light to determine if the velocity of mitochondrial movement can be restored by low level light therapy (LLLT). Axonal transport of labeled mitochondria was documented by time lapse microscopy in dopaminergic PD and CNT cybrid neuronal cells before and after illumination with an 810 nm diode laser (50 mW/cm2) for 40 seconds. Oxygen utilization and assembly of mtETC complexes were also determined.

RESULTS: The velocity of mitochondrial movement in PD cybrid neuronal cells (0.175 +/- 0.005 SEM) was significantly reduced (p < 0.02) compared to mitochondrial movement in disease free CNT cybrid neuronal cells (0.232 +/- 0.017 SEM). For two hours after LLLT, the average velocity of mitochondrial movement in PD cybrid neurites was significantly (p < 0.003) increased (to 0.224 +/- 0.02 SEM) and restored to levels comparable to CNT. Mitochondrial movement in CNT cybrid neurites was unaltered by LLLT (0.232 +/- 0.017 SEM). Assembly of complexes in the mtETC was reduced and oxygen utilization was altered in PD cybrid neuronal cells. PD cybrid neuronal cell lines with the most dysfunctional mtETC assembly and oxygen utilization profiles were least responsive to LLLT.

CONCLUSION: The results from this study support our proposal that axonal transport is reduced in sporadic PD and that a single, brief treatment with near-infrared light can restore axonal transport to control levels. These results are the first demonstration that LLLT can increase axonal transport in model human dopaminergic neuronal cells and they suggest that LLLT could be developed as a novel treatment to improve neuronal function in patients with PD.

Pretreatment with near-infrared light via light-emitting diode provides added benefit against rotenone- and MPP+-induced neurotoxicity.

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Parkinson’s disease (PD) is a movement disorder caused by the loss of dopaminergic neurons in the substantia nigra pars compacta, leading to nigrostriatal degeneration. The inhibition of mitochondrial respiratory chain complex I and oxidative stress-induced damage have been implicated in the pathogenesis of PD. The present study used these specific mitochondrial complex I inhibitors (rotenone and 1-methyl-4-phenylpyridinium or MPP(+) on striatal and cortical neurons in culture. The goal was to test our hypothesis that pretreatment with near-infrared light (NIR) via light-emitting diode (LED) had a greater beneficial effect on primary neurons grown in media with rotenone or MPP(+) than those with or without LED treatment during exposure to poisons. Striatal and visual cortical neurons from newborn rats were cultured in a media with or without 200 nM of rotenone or 250 microM of MPP(+) for 48 h. They were treated with NIR-LED twice a day before, during, and both before and during the exposure to the poison.

Results: indicate that pretreatment with NIR-LED significantly suppressed rotenone- or MPP(+) induced apoptosis in both striatal and cortical neurons (P<0.001), and that pretreatment plus LED treatment during neurotoxin exposure was significantly better than LED treatment alone during exposure to neurotoxins. In addition, MPP(+) induced a decrease in neuronal ATP levels (to 48% of control level) that was reversed significantly to 70% of control by NIR-LED pretreatment. These data suggest that LED pretreatment is an effective adjunct preventative therapy in rescuing neurons from neurotoxins linked to PD.


Near-infrared light via light-emitting diode treatment is therapeutic against rotenone- and 1-methyl-4-phenylpyridinium ion-induced neurotoxicity.

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Parkinson’s disease is a common progressive neurodegenerative disorder characterized by the degeneration of dopaminergic neurons in the substantia nigra pars compacta. Mitochondrial dysfunction has been strongly implicated in the pathogenesis of Parkinson’s disease. Thus, therapeutic approaches that improve mitochondrial function may prove to be beneficial. Previously, we have documented that near-infrared light via light-emitting diode (LED) treatment was therapeutic to neurons functionally inactivated by tetrodotoxin, potassium cyanide (KCN), or methanol intoxication, and LED pretreatment rescued neurons from KCN-induced apoptotic cell death. The current study tested our hypothesis that LED treatment can protect neurons from both rotenone- and MPP(+)-induced neurotoxicity. Primary cultures of postnatal rat striatal and cortical neurons served as models, and the optimal frequency of LED treatment per day was also determined.

Results: indicated that LED treatments twice a day significantly increased cellular adenosine triphosphate content, decreased the number of neurons undergoing cell death, and significantly
reduced the expressions of reactive oxygen species and reactive nitrogen species in rotenone- or MPP(+) exposed neurons as compared with untreated ones. **These results strongly suggest that LED treatment may be therapeutic to neurons damaged by neurotoxins linked to Parkinson’s disease by energizing the cells and increasing their viability.**


**Mitochondrial signal transduction in accelerated wound and retinal healing by near-infrared light therapy.**


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Photobiomodulation by light in the red to near infrared range (630-1000 nm) using low energy lasers or light-emitting diode (LED) arrays has been shown to accelerate wound healing, improve recovery from ischemic injury in the heart and attenuate degeneration in the injured optic nerve.

Recent evidence indicates that the therapeutic effects of red to near infrared light result, in part, from intracellular signaling mechanisms triggered by the interaction of NIR light with the mitochondrial photoacceptor molecule cytochrome c oxidase.

We have demonstrated that NIR-LED photo-irradiation increases the production of cytochrome oxidase in cultured primary neurons and reverses the reduction of cytochrome oxidase activity produced by metabolic inhibitors.

We have also shown that NIR-LED treatment prevents the development of oral mucositis in pediatric bone marrow transplant patients. Photobiomodulation improves wound healing in genetically diabetic mice by upregulating genes important in the promotion of wound healing.

More recent studies have provided evidence for the therapeutic benefit of NIR-LED treatment in the survival and functional recovery of the retina and optic nerve in vivo after acute injury by the mitochondrial toxin, formic acid generated in the course of methanol intoxication.

Gene discovery studies conducted using microarray technology documented a significant upregulation of gene expression in pathways involved in mitochondrial energy production and antioxidant cellular protection.

These findings provide a link between the actions of red to near infrared light on mitochondrial oxidative metabolism in vitro and cell injury in vivo.

Based on these findings and the strong evidence that mitochondrial dysfunction is involved in the pathogenesis of numerous diseases processes, we propose that NIR-LED photobiomodulation represents an innovative and non-invasive therapeutic approach for the treatment of tissue injury and disease processes in which mitochondrial dysfunction is postulated to play a role including diabetic retinopathy, age-related macular degeneration, Leber’s hereditary optic neuropathy and Parkinson’s disease.