Near-infrared laser therapy promotes recovery of damaged neurons

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Photobiostimulation is a novel noninvasive method to help protect neurons and repair injured neuronal pathways.

When a person suffers an ischemic stroke, the type in which a blood clot blocks an artery in the brain, oxygen-starved cells at the epicenter of the injury quickly perish. In the hours following the onset of the stroke, neurons in a larger affected area called the penumbra remain in danger of suffering severe harm or dying, greatly worsening the patient’s prognosis. Yet only one therapeutic agent has been approved by the Food and Drug Administration for use in cases of ischemic stroke, and it has a somewhat limited effectiveness and is accompanied by a significant risk of brain hemorrhage. Thus, there is a great need for new therapies to protect neurons and other cells from the detrimental effects of ischemia, and promote their functional recovery from stroke-induced damage. A novel noninvasive treatment that has been studied for over a decade is transcranial near-infrared laser therapy (NILT), which uses light that penetrates through the intact skull to activate neuroprotection and recovery processes.

Also known as photobiostimulation, NILT has been studied in both animals and humans (see Figure 1). Extensive preclinical and clinical studies have shown NILT to be an effective treatment for acute ischemic stroke (AIS). In laboratory settings, NILT is also being developed as a possible treatment for traumatic brain injury (TBI), Alzheimer’s disease, and Parkinson’s disease. Some intriguing data suggests that NILT may promote clinical improvement in neurodegenerative diseases, such as these, in which dysfunction of mitochondria (the powerhouses within cells) and consequent energy impairment play a role.

We have used NILT to develop treatment regimens that can be transferred from the laboratory to the clinic and back again to the laboratory for refinement. Initially we focused on continuous wave (CW) NILT, in which the laser shines at a constant low power for a period of minutes. We showed that CW NILT was beneficial to specific populations of stroke patients. However, we now see that CW NILT has limitations, primarily associated with low energy penetration to deeper brain regions, which may reduce the treatment’s efficacy in patients. To enhance NILT’s efficacy, we are developing pulse wave (PW) treatment regimens. In one regimen, for example, the laser produces 2ms pulses at a rate of 100Hz. The goals of using PW NILT are to enhance the penetration of photons to deep brain structures and to maximally increase mitochondrial function.

The current hypothesis for NILT’s efficacy is based upon a two-step process: the light first elicits an acute response, followed by a chronic response in which activation of neuronal survival and plasticity mechanisms achieves a long-term effect. These responses are not related to heating of tissue, which is minimal, but appear to be wavelength-specific, being effective when NILT is used at wavelengths of 630nm or 808nm. Both of these wavelengths correspond to absorption peaks of a vital mitochondrial enzyme called cytochrome c oxidase (COX).

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The acute phase response by photobiostimulation directly affects cellular metabolic activity regulated within mitochondria. Specifically, NILT increases adenosine triphosphate (ATP) formation in brain cells after COX (and perhaps other enzymes) absorb photons of the light. ATP is the unit of fuel that delivers the energy needed by innumerable cellular processes. Usually mitochondria produce ATP efficiently by aerobic respiration. In AIS or TBI, neuronal tissue deprived of oxygen may survive for some time by switching to less-efficient anaerobic respiration. We hypothesize that the mitochondrial stimulation by NILT may help cells to switch back to aerobic respiration, improving the cell’s chances for recovery. In AIS, NILT may also increase cerebral blood flow, which ultimately allows cells to receive more oxygen and nutrients.

The chronic response of NILT appears to have long-term effects by also increasing RNA transcription and protein synthesis, activating mechanisms that aid in alleviating injury-induced brain dysfunction. NILT may have a direct or indirect effect on synaptic plasticity and possibly neurogenesis. In addition, NILT-induced suppression of inflammatory responses may be partly responsible for chronic effects of the treatment. Animal studies have shown NILT to be neuroprotective and able to restore function following various brain insults and in various diseases, such as TBI, Alzheimer’s, and Parkinson’s. Common mechanisms may underlie NILT’s beneficial effects on neuronal survival and enhanced clinical function in these disparate pathologies.

Building on the promising results from years of translational research, we are currently probing the mechanism of NILT at the cellular level to better understand and optimize the use of NILT to treat various acute and chronic brain insults. Furthermore, we will differentiate between CW and PW NILT using biochemical methodology and behavioral assays in animal studies. In conclusion, rigorous research in animal models of neurodegenerative diseases is slowly being translated into well-designed clinical trials to apply NILT to attenuate and even reverse deficits associated with neuronal damage. Given the fast pace of research in this area, we expect many more clinical trials will be initiated to test NILT strategies in humans.

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References