Understand the benefits and science behind mTBI treatments

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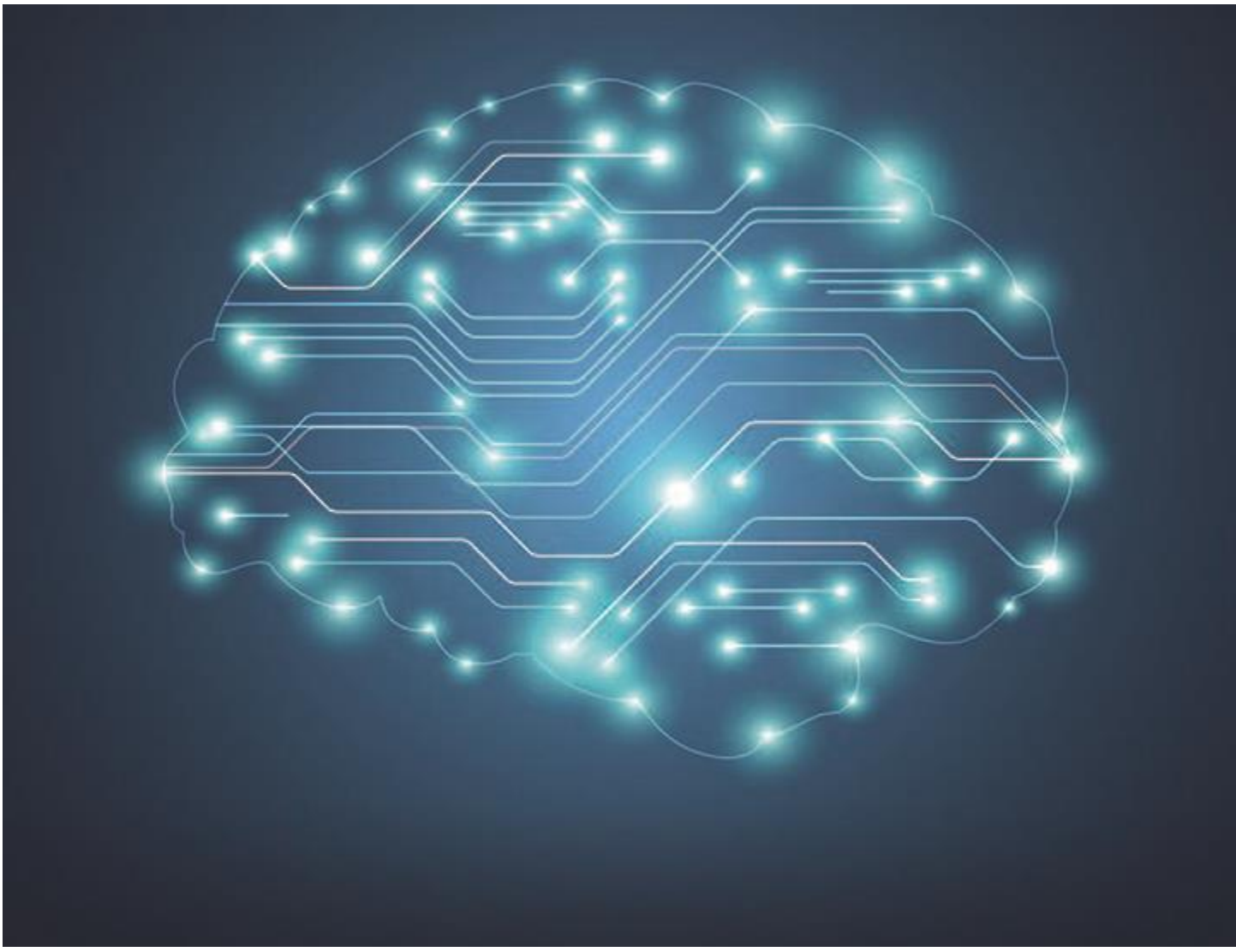

The use of transcranial low level laser therapy (tLLLT) finding increasing acceptance in the treatment and management of neurodegenerative diseases and mild traumatic brain injury (mTBI.)

The fact that tLLLT can be effectively employed using the near-infrared low level lasers already found in many chiropractic offices allows doctors of chiropractic to be instrumental in the early management of mTBI patients.

Essential to good therapeutic outcomes is a basic understanding of biostimulation, clinical benefits, and individual laser equipment used in the treatment of mTBI.

Mitochondrial biostimulation

Before addressing the clinical benefits of tLLLT, it will be helpful to understand how the therapeutic use of near- infrared laser light affects the cell. The following is a brief review of the mitochondrial biology affected by the mechanics of photobiostimulation. Cytochrome c oxidase (COX) is Complex IV and the terminal enzyme of the electron transport chain. It plays a vital role in the bioenergetics of a cell.

COX is a multicomponent membrane protein that contains a binuclear copper center along with a heme binuclear center, both of which facilitate the transfer of electrons from COX to oxygen. Generally speaking, COX can be in three states: fully oxidized, fully reduced, or as a partially reduced enzyme, usually called mixed-valence one. The mixed valence has some metal centers in their higher oxidation state, and the remainder in their lower oxidation state. COX cannot be considered as a primary photoreceptor when it is fully oxidized or fully reduced, but only when it is in one of the mixed valence states.

In the simplest terms, light is delivered in energy packets called photons. Photon energy is the energy carried by a single photon with a certain electromagnetic wavelength and frequency. Photons are absorbed by delocalized electron pi clouds of complex aromatic molecules (i.e., heme) with matching wavelengths, exciting them to a higher energy state. This energy is passed to the metalloprotein centers. When the energy excitement is high enough, the metal center releases an electron reducing the metal center. This is the initialization of photobiostimulation.

The near-infrared (NIR) spectrum of 600 to 1,000 nm is the photobiostimulation light spectrum. The mid 600 nm and low 800 nm spectra have been shown to have the most beneficial effects in recent research although some higher wavelengths have been reported to offer benefit.

It is known that LLLT reverses both states of COX-related mitochondrial dysfunction: excessive reduction and excessive oxidation COX. When exposed to LLLT, COX becomes a new source of highly energized electrons.

These newly released electrons can be accepted by NAD and FAD at Complexes I and II to re-energize the electron transport chain (ETC) in the hypoxic state of the injured cell's mitochondria.

A "closed loop" forms as electrons are recirculated instead of attaching to O2 and disappearing. At the same time, Complexes I and III maintain the proton pump and thereby restore the production of needed ATP in stressed and injured cells. It does this without the damaging effects

of excess super- oxide anion production that would normally be expected from an up- regulation of ATP production required by injured cells.

In effect, this is mitochondrial resuscitation and it allows mitochondria to break the “vicious cycle” of dysfunction and start the process of recovery through a cascade of beneficial cellular activity. Through this mechanism, post-brain-injury changes to hemodynamics, inflammation, the resulting hypoxia, and decreased ATP production are addressed in the mitochondria of neurons.

Tau protein pathology

Brain trauma results in stressed, hypoxic neurons. Left untreated, the resulting acute state of hypoxia can lead to complex and vicious cycles involving various regions of the brain. These include a breakdown of the blood- brain barrier, glial cell priming, neuroinflammation, tau protein formation, dysautonomia, immunological and metabolic imbalances, and even GI dysregulation via vagal influence.

Tau proteins rapidly form after neuronal injury and death as a result of the aforementioned mitochondrial stress. They have been shown to be toxic to surrounding neurons and glial cells. Tau oligomers initiate the spread of tau pathology in the brain. Tau oligomers precede the formation of neurofibrillary tangles (NFT) and contribute to learning and memory deficits (and even neuronal cell death). Tauproteinopathies can be induced by single or repetitive TBI and often lead to progressive neurodegeneration as seen in progressive supranuclear palsy, dementia, and Alzheimer’s disease.

Photobiostimulation can have a powerful mitigating influence on the formation of tau proteins associated with traumatic encephalopathy and progressive neurodegeneration. It has been shown to reverse deposition in some instances, especially in early or immature tau protein deposits.

Clinical effects of tLLLT

It is important to remember that once the brain is injured, even a short period of ischemia can cause significant physiological changes with chronic sequelae. This emphasizes the importance of early intervention with mTBI and concussion injuries to minimize long-term risk.

Early intervention with tLLLT can effectively address metabolic and biochemical variables to help stabilize and reduce the area of brain injury. As mentioned, it increases oxidative phosphorylation (OXPHOS) energy production in hypoxic tissue without a corresponding increase in mitochondrial reactive oxygen species (ROS.) The result is prevention of additional or secondary loss of stressed and injured neurons, thereby limiting the area of lesion as well as activating brain repair pathways. A reduction in cognitive deficits is also a reported benefit of tLLLT.

From a neurobiological perspective, the cascade of beneficial cellular activity includes increased mitochondrial membrane potential, nitric oxide release, and the modulation of intracellular calcium. Signaling pathways and transcription factors are activated, leading to production of

anti-apoptotic, pro-proliferation, antioxidant, anti-inflammatory, and proangiogenic factors. The regeneration of neurons through neurogenesis and synaptogenesis aids in the restoration and maintenance of cognitive function and supports neuroplasticity during the recovery process.

Brain repair is directly affected by the expression of genes related to cell proliferation and indirectly through regulation of the expression of genes related to cell migration and remodeling, DNA synthesis and repair, ion channel and membrane potential, cell metabolism, and suppression of apoptosis.

Cognitive function benefits by stimulation of these brain repair pathways and reduction of NFT. Neuroplasticity is supported by an increase in brain-derived neurotrophic factor (BDNF) and synapsin-1 that encourages synaptogenesis and is significantly upregulated by photobiostimulation.

This should be of tremendous benefit for both synaptic and non-synaptic neuroplastic change, which has significant implications for post-traumatic learning, memory, and recovery from brain damage. Moreover, these effects in the brain suggest tLLLT may have wider applications in neurodegenerative and psychiatric disorders.

Clinical considerations for tLLLT

Clinicians working with laser biostimulation should know the amount of photon energy (i.e., dosage) measured in mW/cm2 or J/cm2 being delivered to the brain. Power and wavelength options will vary between various units and manufacturers. The delivery of the photon energy will vary depending on wavelength, power, and time to determine penetration and depth of the target tissue dose.

Under- and overstimulation with low level laser application often fails to achieve the desired effect in tissue by either failing to reach the necessary stimulatory threshold or exceeding biostimulatory capacity and triggering inhibitory and braking mechanisms within the ETC, mitochondria, and cell. Effective tissue dose thresholds determined by research points to levels below 10 J/cm2 with 1–1.2 J/cm2 considered optimum for maximum COX activity.

Cadaver studies demonstrate that penetration of laser light varies with the wavelength and, in the 800-to- 1,000 nm range common to lasers used in chiropractic offices, is about 2 percent. For example, depending on the unit’s power and other factors, an 810 nm laser array may need to deliver about 60 J/cm2 transcranially to reach a brain tissue irradiance of 1–1.2 J/cm2.

Laser manufacturers can provide tissue penetration parameters for their laser units and should take into consideration the parameters mentioned here. Calculation of an individual transcranial therapeutic dose should be made by the clinician to achieve the desired 1–1.2 J/cm2 threshold at the depth of the desired tissue to be treated. These should be recorded in the patient’s chart.

Fortunately, tLLLT has been shown to be an extremely safe modality. Over- stimulation, while failing to provide therapeutic benefit, does not adversely affect recovery when compared to no

laser treatment. Additionally, tLLLT does not adversely affect healthy neurons, so early intervention safety is not an issue.

A time for implementation

The standard of medical care for mTBI has largely limited doctors of chiro- practic to diagnosis and supportive measures. But tLLLT is a tool that fills a significant void in the head and neck injury-care paradigm and changes the chiropractor's contribution to integrative model protocols by directly and effectively addressing injury to the CNS in an effective and timely manner.

Considering recent research into the benefit of tLLLT for mTBI, as well as its safety, it is arguably time to remedy an undertreated aspect of chiropractic's approach to traumatic neuromusculoskeletal patient care.

[Editor's note: This is the second part of a two-part series exploring this topic. Part 1 can be read in the Vol. 63, No. 1 edition of Chiropractic Economics, cover date Jan. 20, 2017, or viewed online at ChiroEco.com/mild-traumatic-brain-injury.]

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