Topics

01

Definitions + History

What is photobiomodulation?

02

Mechanisms

How does it work?

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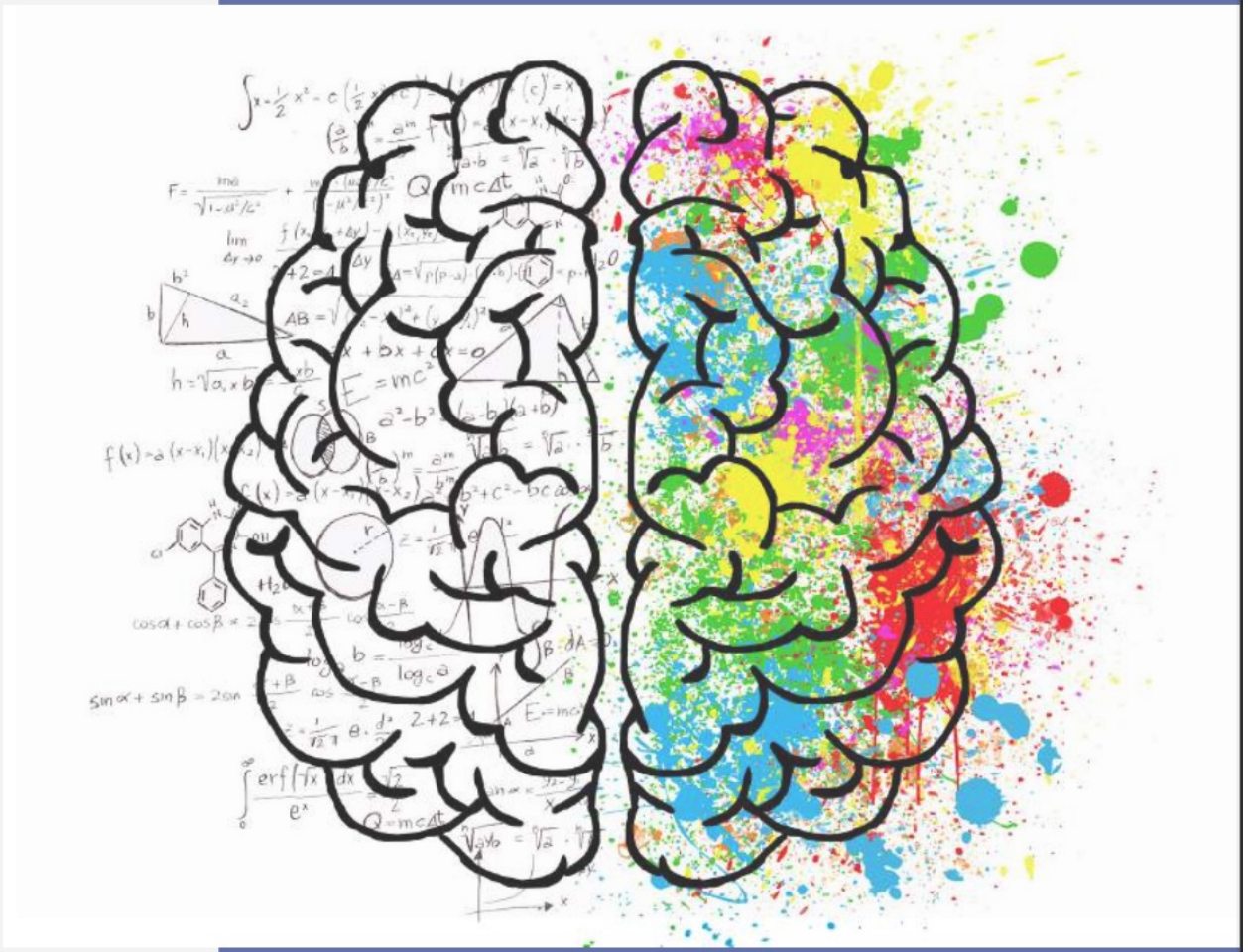
Effects

What are the main effects?

04

Treatment Protocol

How to use?



What's in the name?

LASER (light amplification by stimulated emission of radiation)

Low Level laser therapy
Low Intensive laser therapy
Low energy laser irradiation

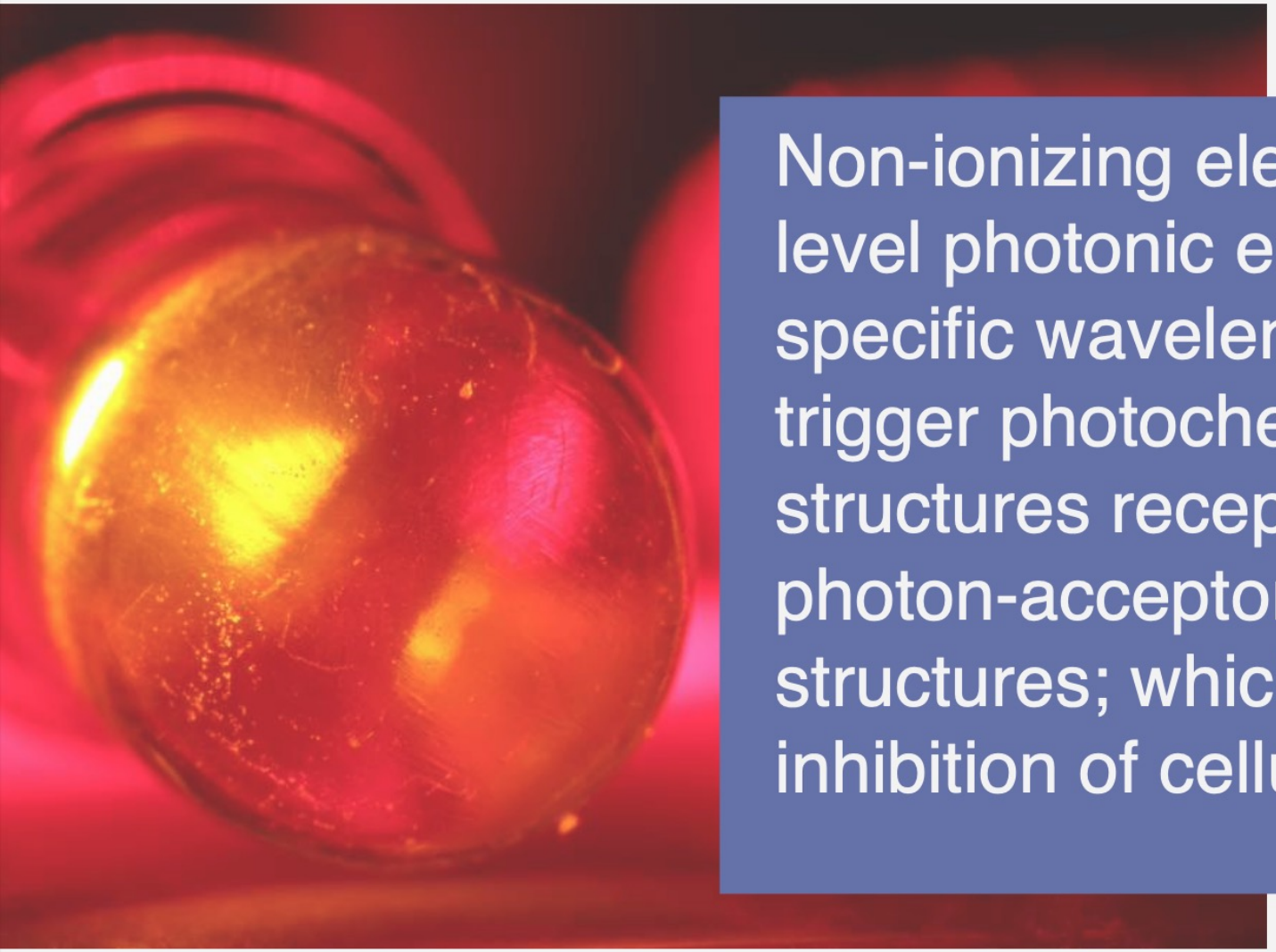
LED (light-emitting diodes)
LEDT (light-emitting diodes therapy)

LOW LEVEL LIGHT THERAPY

LLLP (LOW-LEVEL LIGHT PHOTOBIOMODULATION)

PHOTOBIOSTIMULATION or PHOTOBIOMODULATION

Photobiomodulation

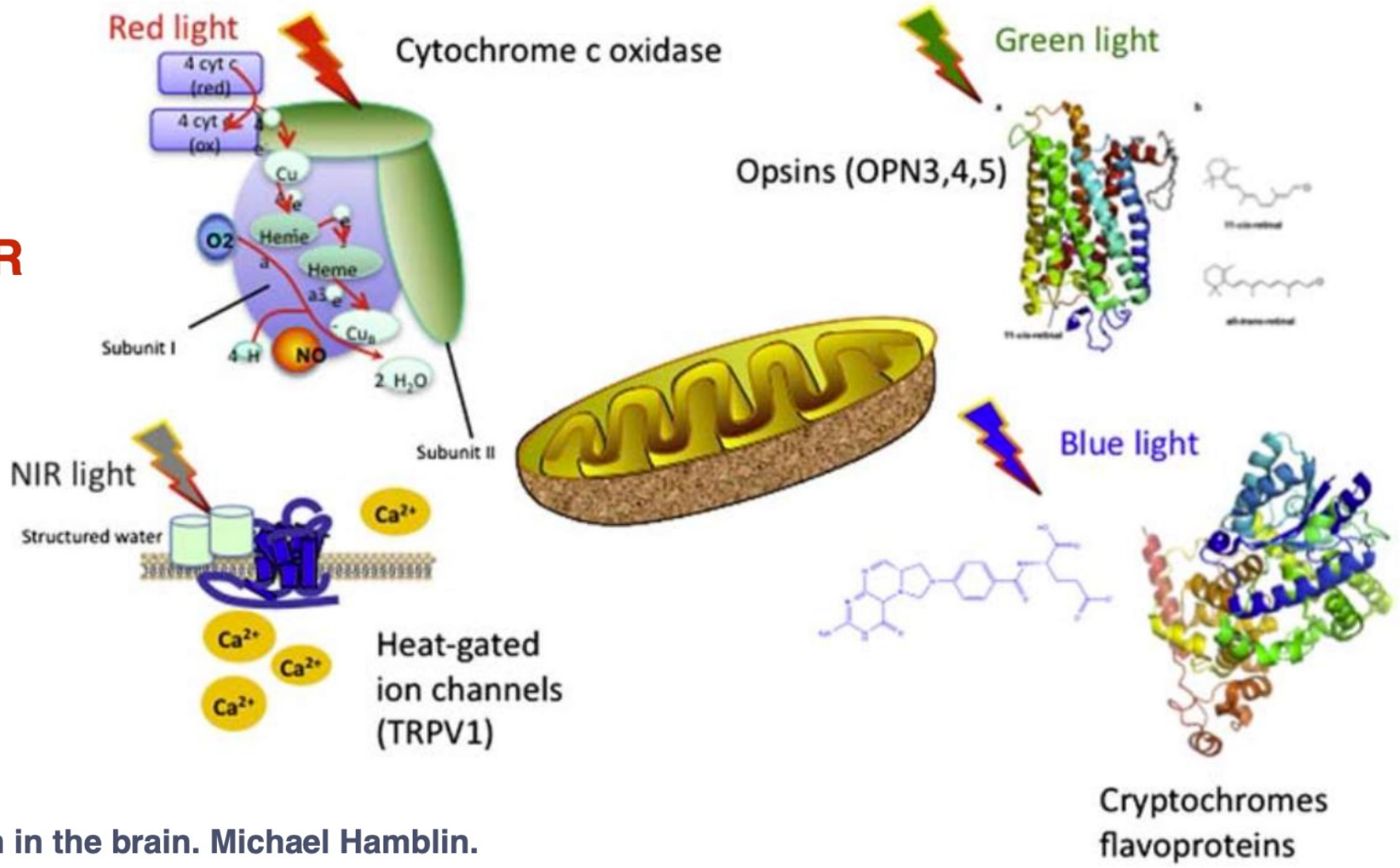


Non-ionizing electromagnetic energy (low-level photonic emissions typically within a specific wavelength range ~300-1000 nm) to trigger photochemical changes within cellular structures receptive to photons: the so-called photon-acceptors or photon-sensitive structures; which lead to stimulation or inhibition of cellular and biological processes.

CIDRAL-FILHO. CHAPTER: LOW-LEVEL LIGHT PHOTOBIOMODULATION. BOOK: INTEGRATIVE PHYSICAL THERAPY, 2019.

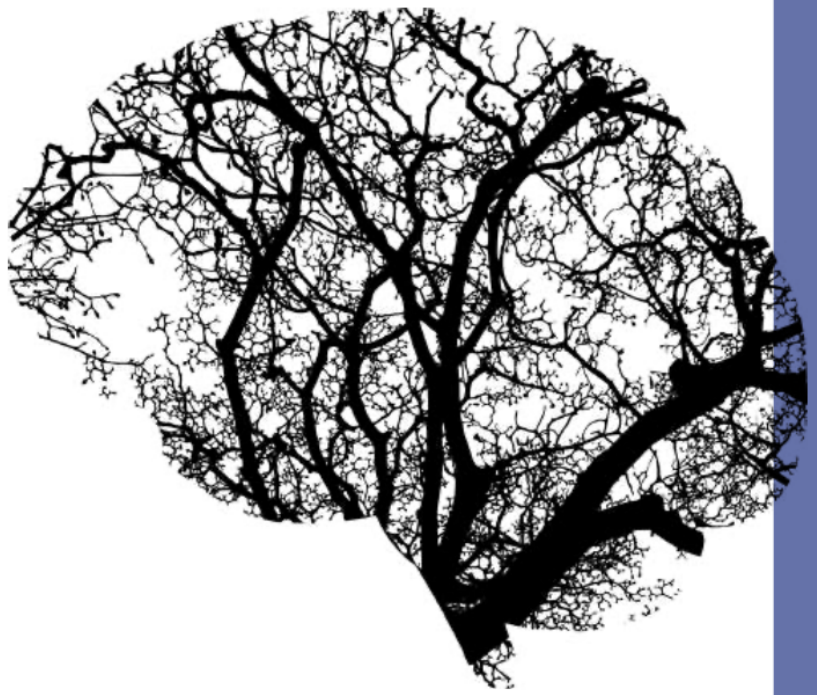
Photon-acceptors or photon-sensitive structures

RED / NIR



Photobiomodulation in the brain. Michael Hamblin.

Transcranial Photobiomodulation (tPBM)



"Transcranial photobiomodulation (t-PBM) is a novel form of neuromodulation with promising results for the treatment of neuropsychiatric disorders.
t-PBM has a low cost, good safety profile, and it is easy to self-administer".

Transcranial Photobiomodulation For The Management Of Depression: Current Perspectives

Paula Askalsky[1] and Dan V Iosifescu[1,2]

Neuropsychiatric Disease and Treatment

Neuropsychiatr Dis Treat. 2019; 15: 3255–3272.

History of PBM

- **3000 years ago: India** - sunlight was employed for therapeutic purposes as recorded in the sacred Hindu text **Atharva Veda** dating from 1400 BC.
- **18th century:** sporadic reports in the medical literature indicating sunlight to treat a wide variety of different diseases.
- **19th century:** the therapeutic application of sunlight known as **heliotherapy** gradually became popular.
- **1848-1928:** Theobald Adrian Palm discovered the role of sunlight in the prevention of vitamin D deficiency disease.
- **1860-1904:** Nils Ryberg Finsen: **Nobel Prize for Physiology** in 1903 - treatment of lupus vulgaris with UV light.

Figure 2.2 Nils Ryberg Finsen (1860–1904).

Figure 2.3 The Finsen Institute at Rigshospitalet in Copenhagen, Denmark.

History of LLLT. Michael Hamblin.

History of PBM

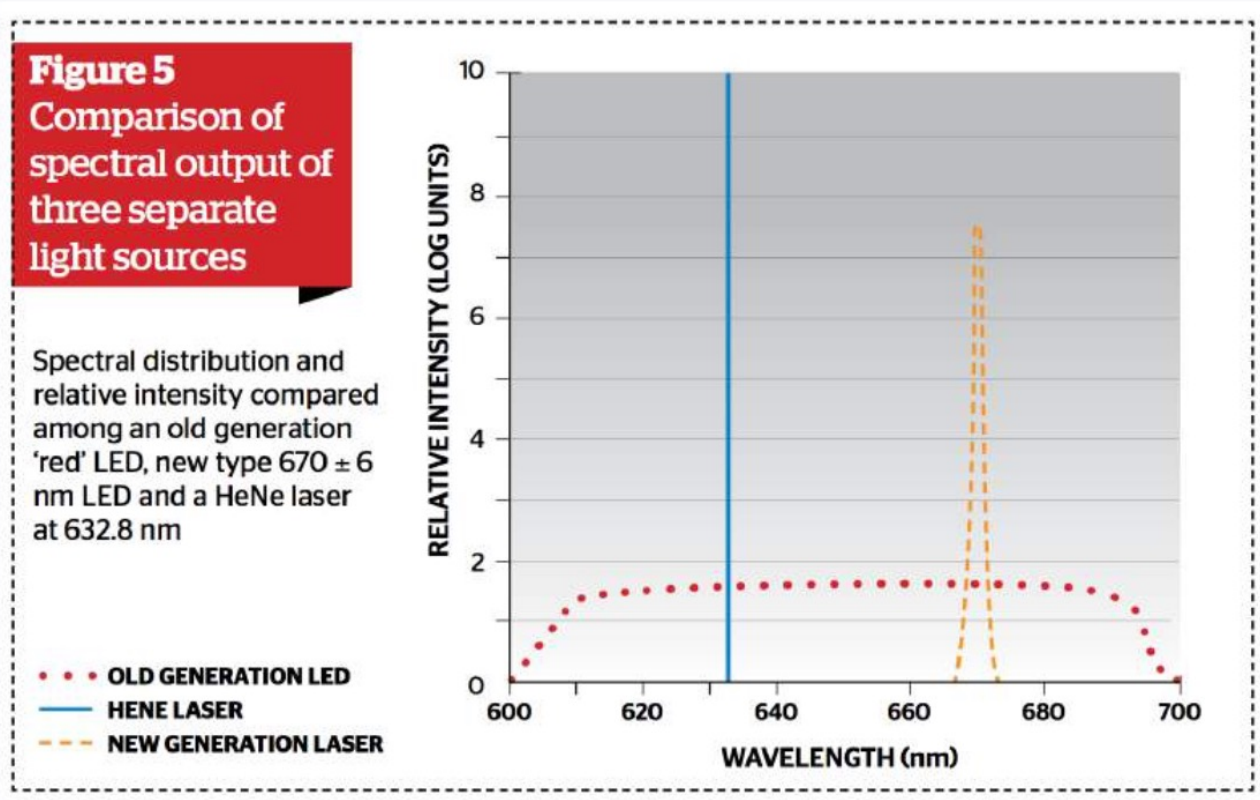
ENDRE MESTER (1903–1984)

- The discovery of **LLLT** can be attributed to Endre Mester (**1903-1984**) in Hungary, who has been called "**the father of photobiomodulation**".

- **1965:** laser research by implanting tumor cells beneath the skin of laboratory rats and exposing them to the beam from a customized ruby laser.
- Tumor cells were not destroyed but instead, the skin incisions healed faster and regrowth of hair was also faster.
- Custom-designed ruby laser was much weaker than originally thought it to be: **low-power laser light**.
- In **1968** he published the first indication of the biphasic dose response of LLLT.

History of PBM

- **1988: National Aeronautic and Space Administration (NASA)** developed the first of a new generation of LEDs, the so-called **NASA LED**.
- Demonstration of the Clinical efficacy of near-infrared LEDs for wound healing.
- The new generation LED was available to researchers and clinicians as a valid therapeutic light source.



LLLT. Glen Calderhead. prime-journal.com. 2016.

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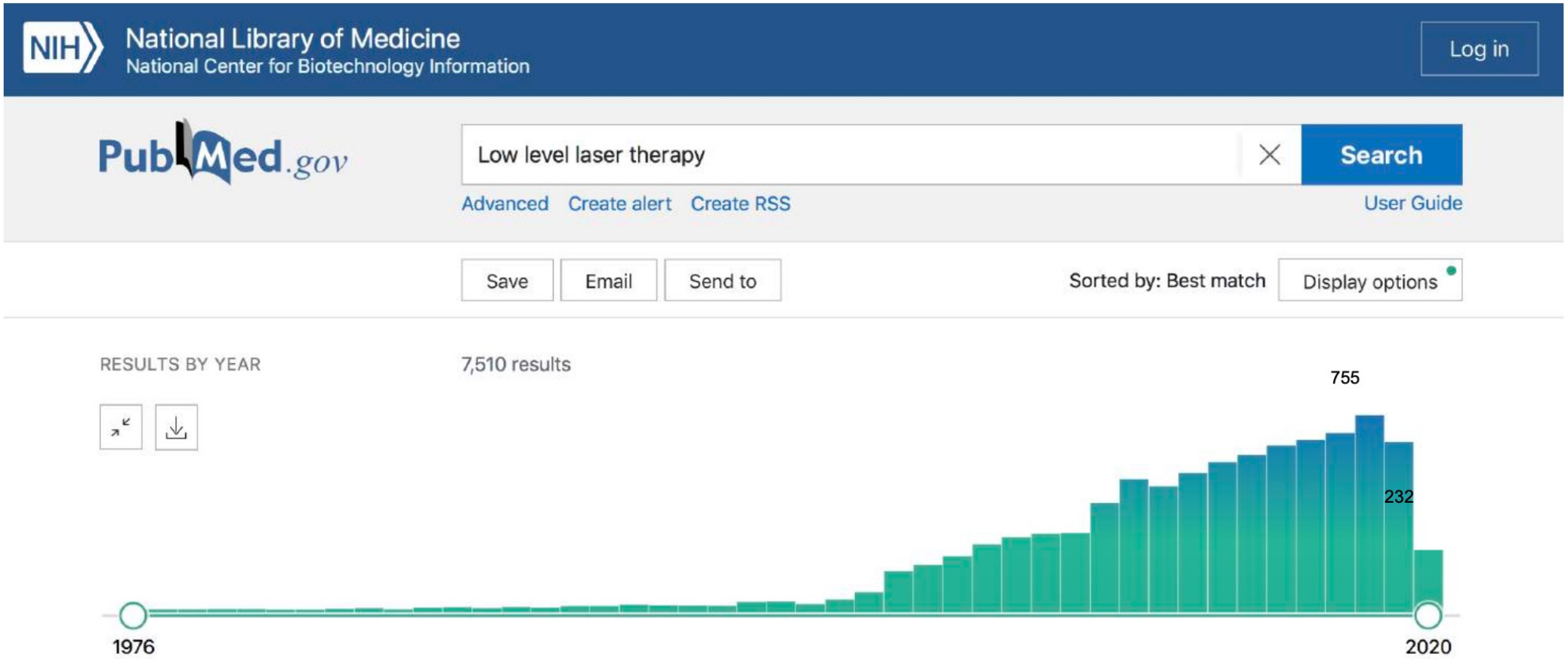
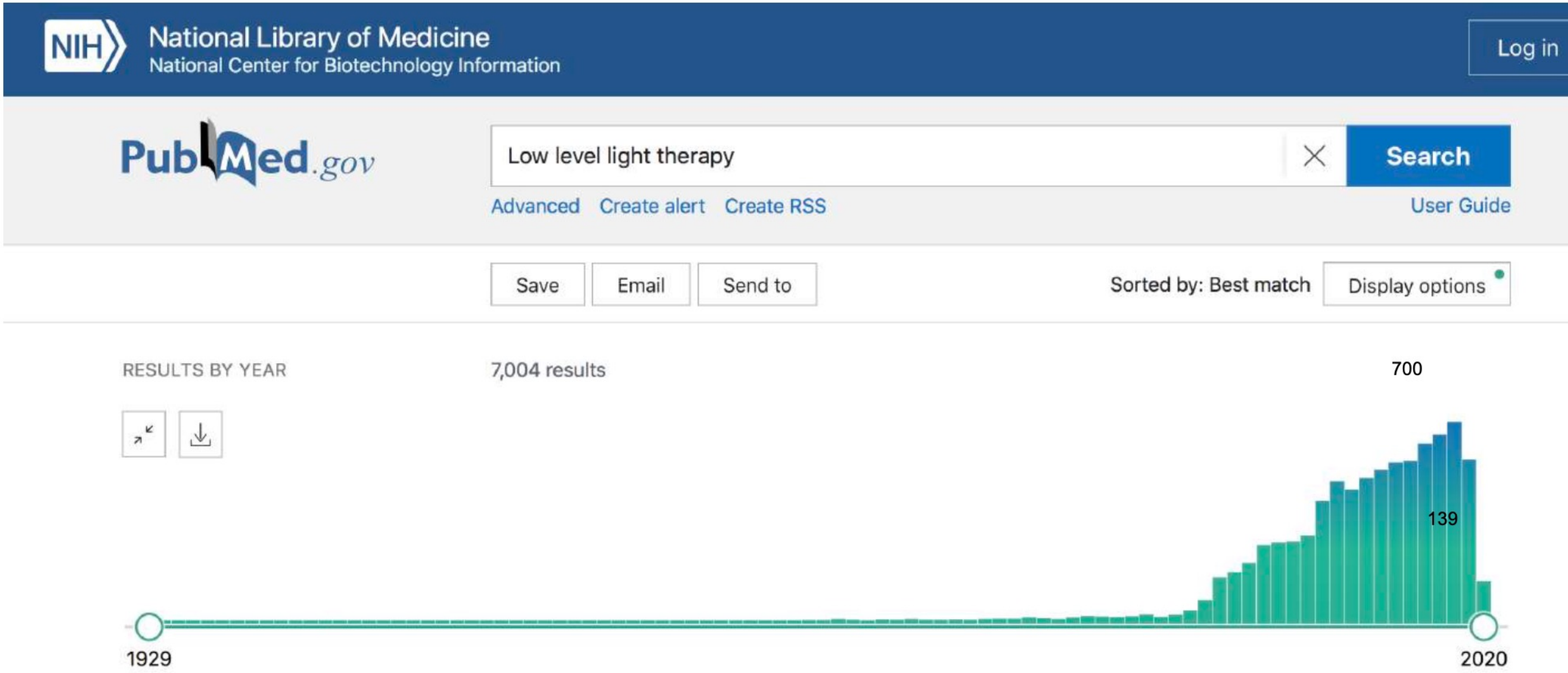
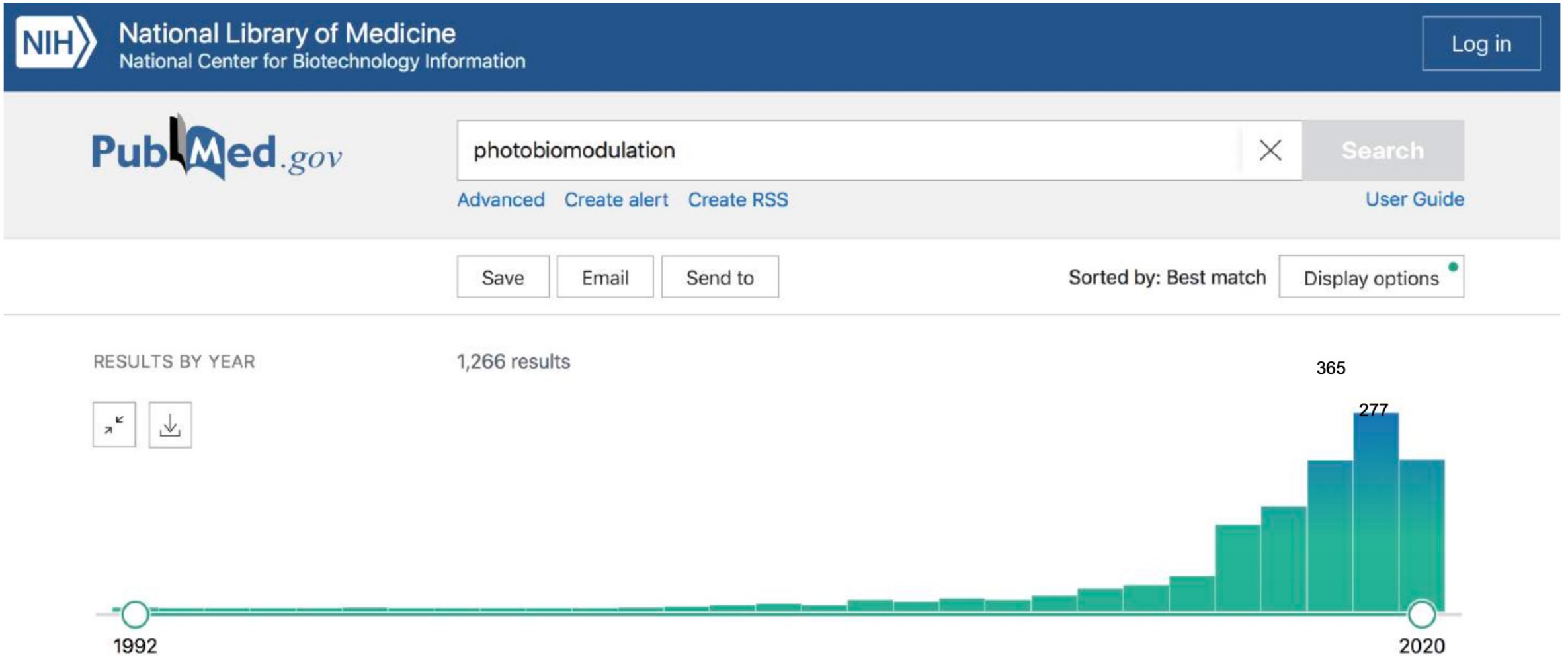
Publications - LLLT



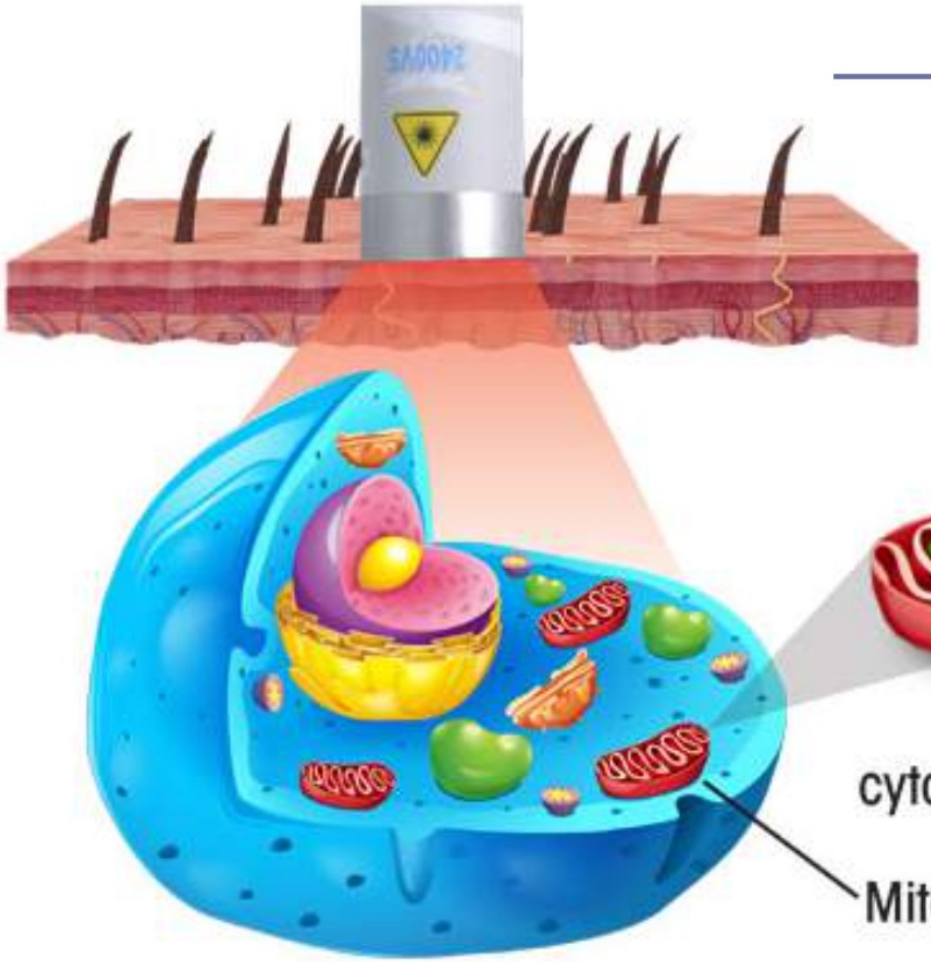
Publications - LLLT



Publications - PBM



Mechanism



cytochrome *c* oxidase

Mitochondria

ATP

An increase in ATP, the main energy source for the majority of cellular functions, **increases the cell's ability to fight infection and accelerates the healing process**

ROS

The modulation of ROS activates transcription factors **positively impacting cellular repair and healing**

NO

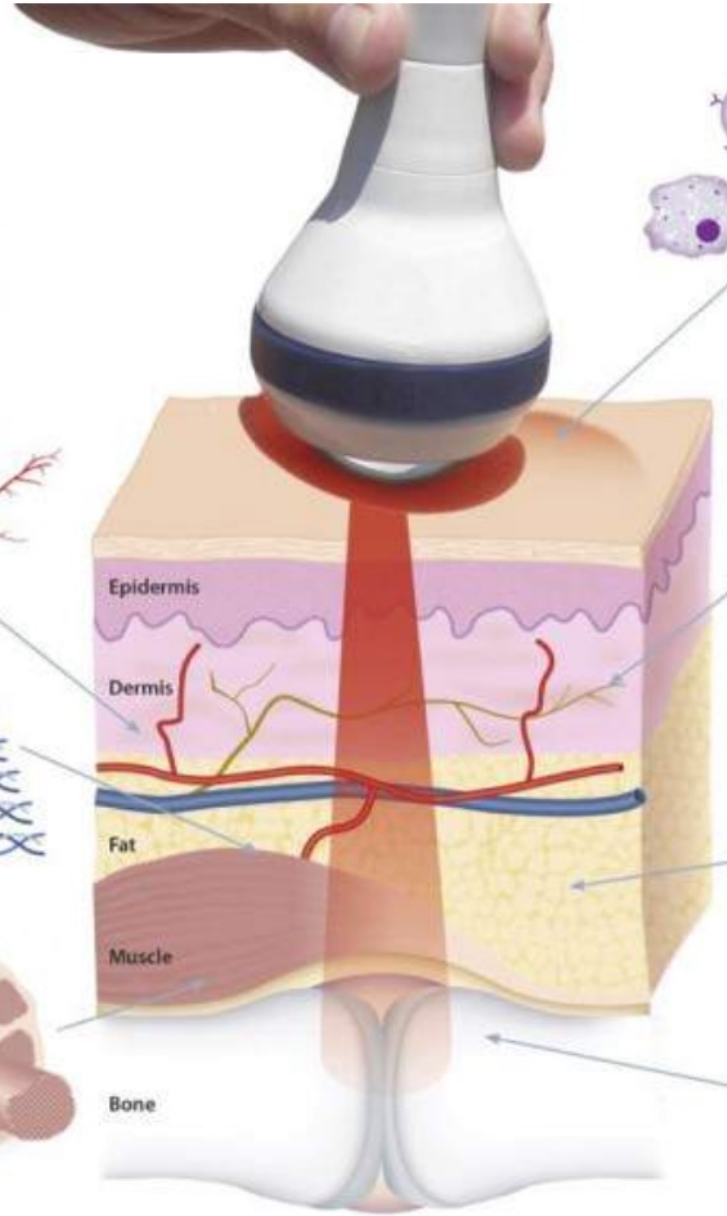
The release of NO, a potent vasodilator, **increases circulation, decreases inflammation** and enhances the **transport of oxygen and immune cells** throughout the tissue

1 Laser light at a wavelength of 670nm, 808nm or 904nm is delivered to the tissue via a probe in **contact mode** with the surface of the skin.

2 The light enters the cell's mitochondria and is absorbed by the chromophores, including the protien cytochrome *c* oxidase (CCO) which then **increases its activity.**

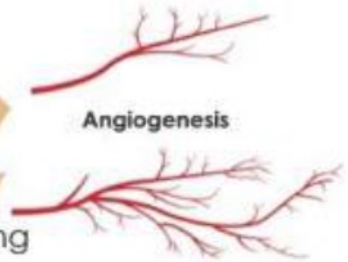
3 As a result of this heightened activity, three molecules are affected: Adenosine Triphosphate (ATP), Reactive Oxygen Species (ROS) and Nitric Oxide (NO)

Overall Clinical Effects



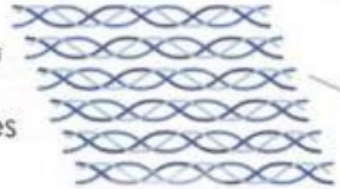
ANGIOGENESIS & NEOVASCULARISATION

An increase in oxygenated blood to the injured tissue accelerates tissue healing



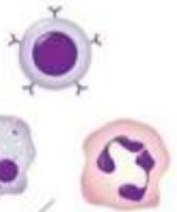
COLLAGEN PRODUCTION

Proper alignment and remodelling of collagen reduces internal scar formation and enhances tissue elasticity



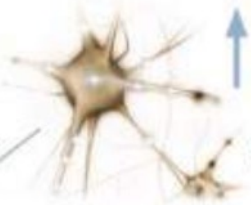
MUSCLE REGENERATION & MUSCLE ATROPHY

Repair of damaged muscle fibres and activation of myogenic satellite cells leads to the regeneration of muscle tissue



INFLAMMATION & OEDEMA

Increase in inflammatory mediators such as macrophages, netrophils and lymphocytes, accelerates and resolves the inflammatory process



NERVE REGENERATION

Proliferation of growth factors promotes neuronal sprouting and myelin formation for optimal nerve recovery

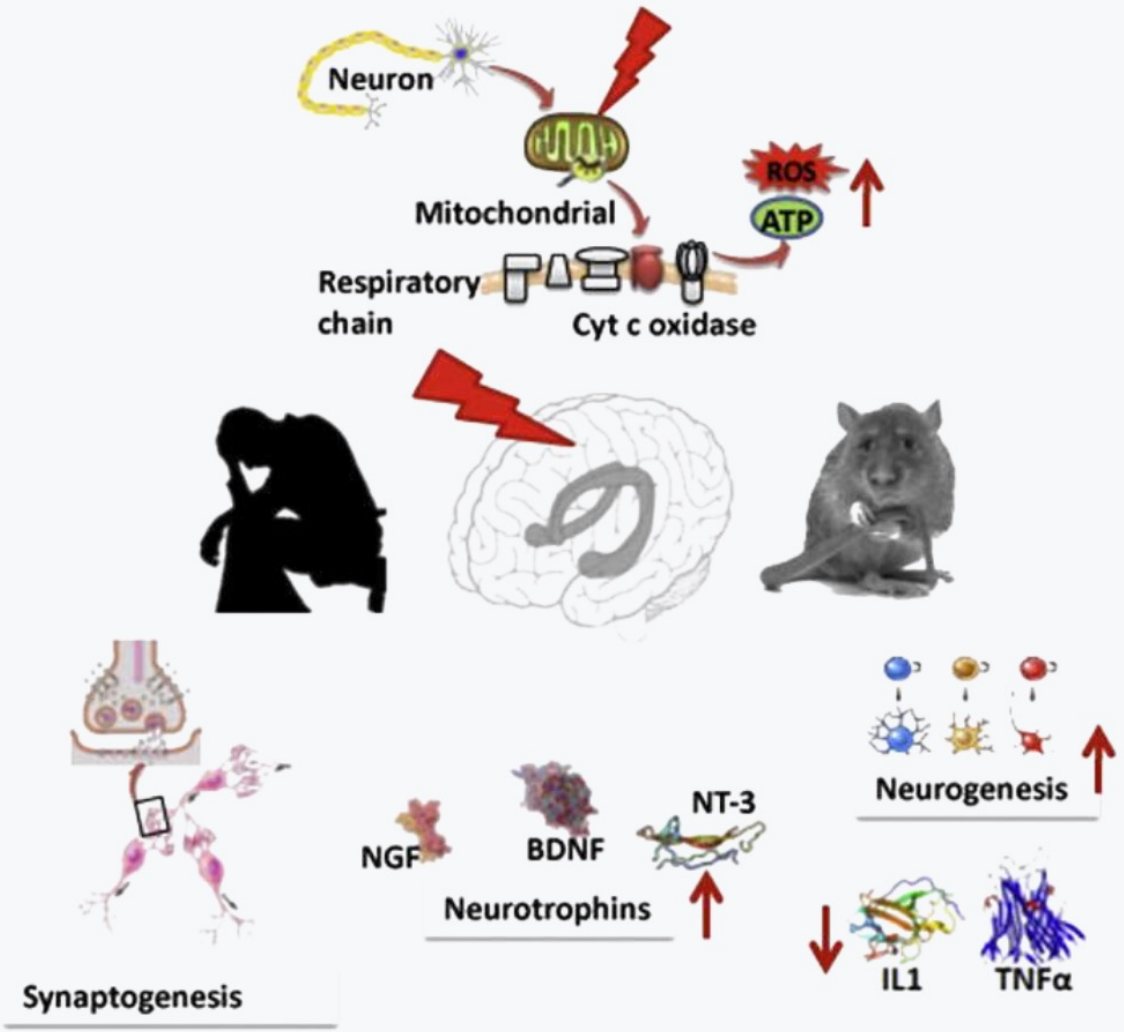
CARTILAGE PRODUCTION

Increase in chondrocyte and collagen production allows for improved cartilage deposition and joint function

BONE FORMATION

Proliferation of osteocytes and remodelling of bone extracellular matrix results in accelerated bone repair

In the Brain



Pro-inflammatory cytokines and neuroinflammation are reduced.

Neurotrophins such as brain-derived neurotrophic factor are upregulated, which in turn activates synaptogenesis (formation of new connections between existing neurons) and neurogenesis (formation of new neurons from neural stem cells).

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Effects of PBM in the Brain

Metabolism

Blood Flow

Neuroprotection

Oxidative Stress

Inflammation

Neurogenesis

Synaptogenesis

Stem Cells

Gamma Rhythms

Improved metabolic functioning through **Increased intracellular ATP production** is one the most strongly supported mechanisms of action.

Metabolism

Several pre-clinical studies have shown that the brain content of ATP is increased by tPBM.

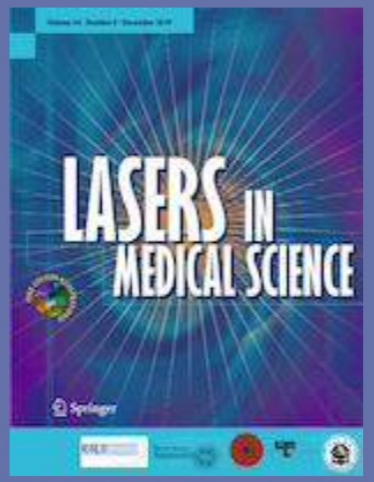
Important: mitochondrial dysfunction, inadequate supplies of ATP, and oxidative stress are contributory factors in almost all forms of brain disease.

This has been reported for neurological conditions **such as major depressive disorder, traumatic brain injury, Parkinson's, and Alzheimer's** (Salehpour et al, 2017).

Blood Flow

One of the changes that is easiest to measure after tPBM, is the change in cerebral blood flow and oxygenation (Wang et al., 2016).

tPBM induces **vasodilation** promoting **improved circulation**, which in turn leads to **improved cerebral oxygenation** (Lee et al., 2017).



Lasers Med Sci. 2015 Jan;30(1):339-46. doi: 10.1007/s10103-014-1669-2. Epub 2014 Oct 3.

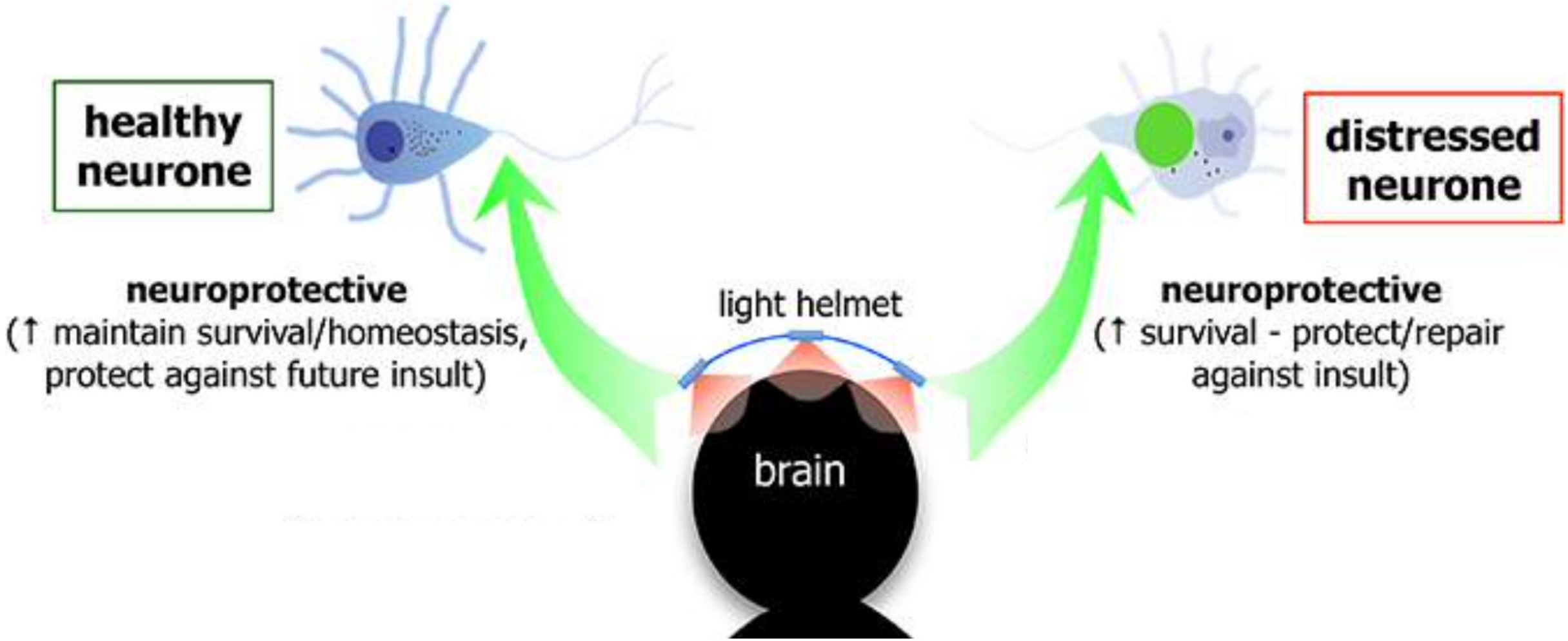
The effects of transcranial LED therapy (TCLT) on cerebral blood flow in the elderly women.

Salgado AS[1], Zângaro RA, Parreira RB, Kerppers II.

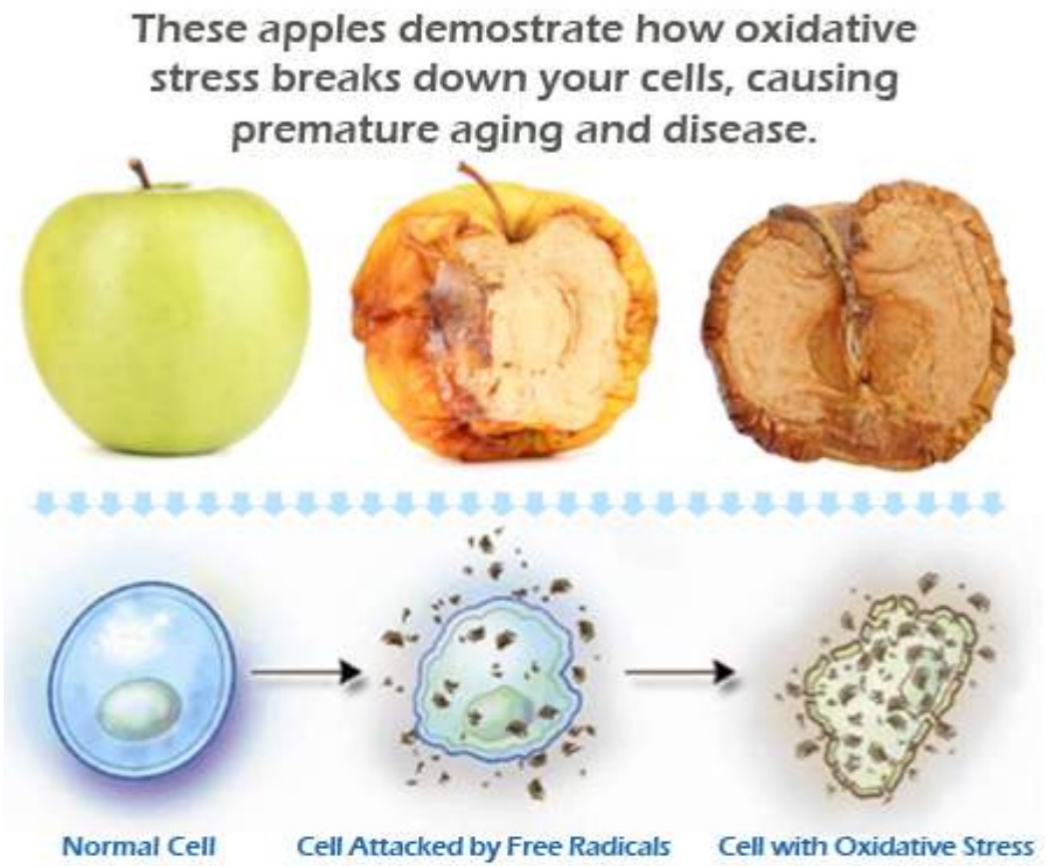
Neuroprotection

Various studies support the use of tPBM for **neuroprotection**, essentially, to protect cells from damage, to promote their survival and longevity, and reverse apoptotic signaling processes.
(Liang et al., 2012).

Neuroprotection



Oxidative Stress



www.endonews.com

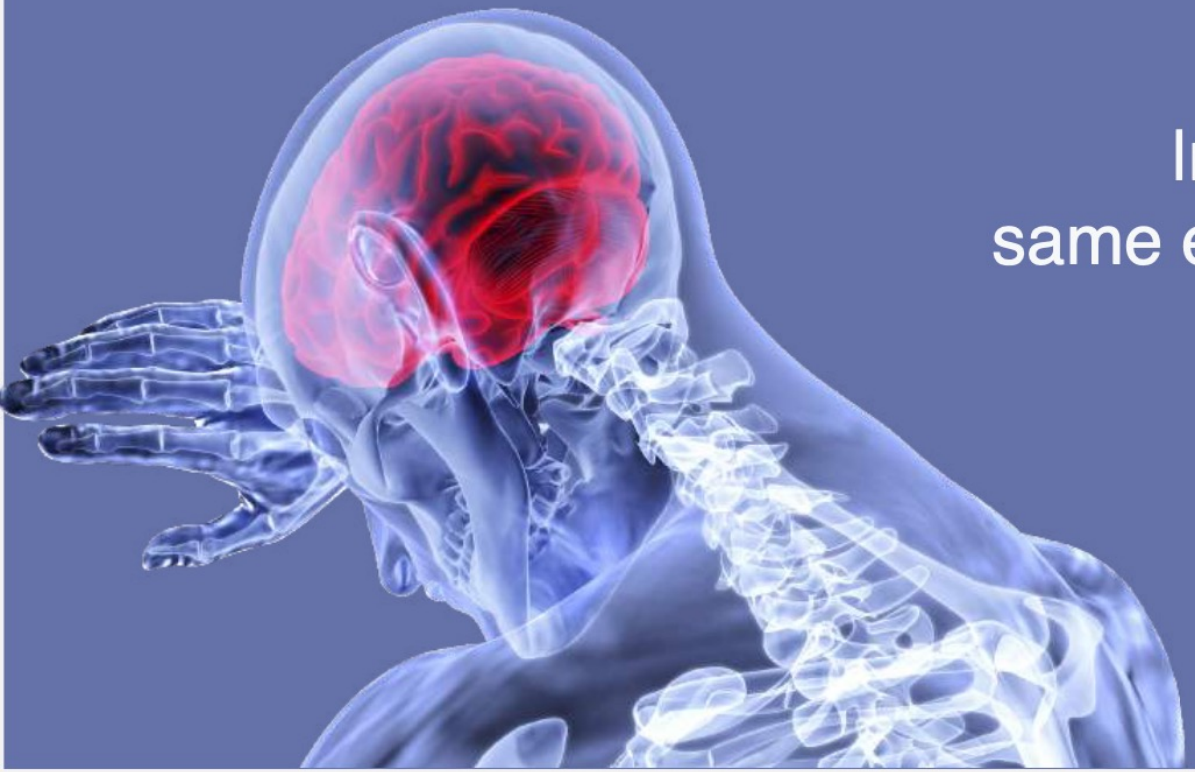
tPBM has marked antioxidant activities (decrease of oxidative stress markers as well increase of anti-oxidative enzymes)

Oxidative stress is linked to various neurological conditions, such as major depressive disorder, traumatic brain injury and Alzheimer's diseases.

(Roomruangwonget al., 2018; Rodríguez et al., 2014; Wu et al., 2014).

Inflammation

tPBM helps reduce inflammation through inhibition of the cyclo-oxygenase 2 (COX-2) enzyme and reduction of inflammatory cytokines (IL-1 and TnF-a), as well as stimulation of expression of anti-inflammatory cytokines (IL-10).



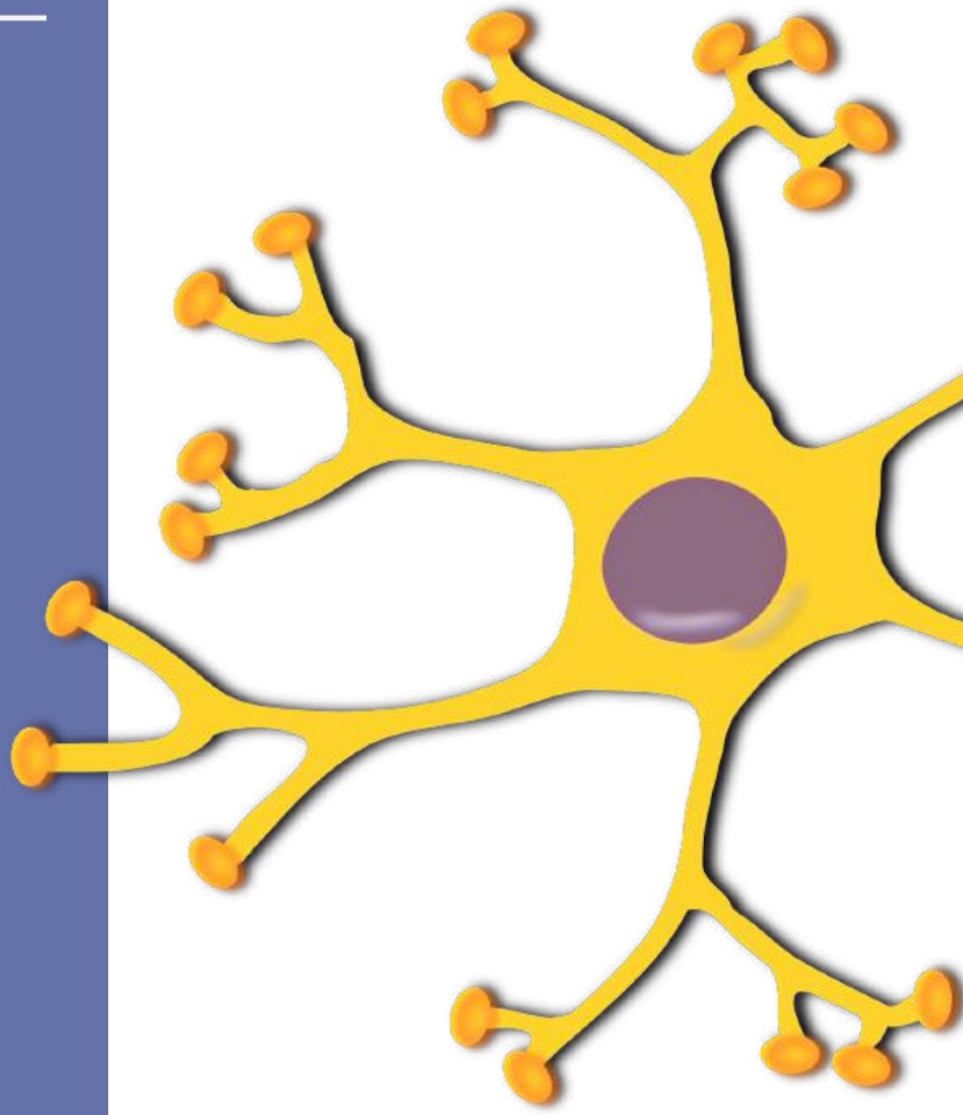
In comparative studies tPBM induced the same effect of anti-inflammatory drugs with no harmful side-effects.

(Lim et al., 2017; yang et al., 2017)

Neurogenesis

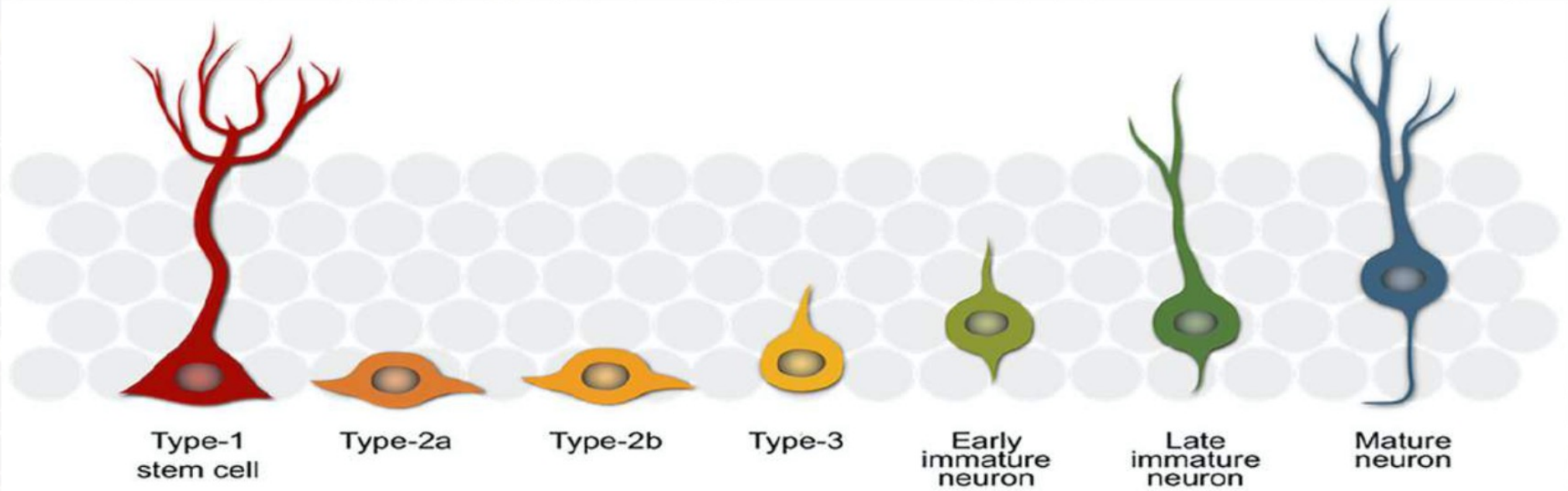
Neurogenesis is mediated by neural stem cells (NSCs) and neuroprogenitor cells throughout our life span (Bergmann et al., 2015; Lepousez et al., 2015).

There is a sharp drop in hippocampal neurogenesis in subjects with AD, and this reduction increased along with disease progression (Moreno-Jiménez et al., 2019)



Neurogenesis

PBM has been show to stimulate Neurogenesis and increase neuronal function (Forrest et al., 2018).



Synaptogenesis

tPBM on the brain has been shown to promote synaptogenesis, also called **neuroplasticity**.

This process is vitally important in many brain conditions, including Traumatic brain injury, stroke, neurodegenerative diseases, and mood disorders.

tPBM has shown to counter these effects by facilitating neural organization, increasing neuroplasticity and synaptogenesis.

(Yan et al., 2017; Barbieri et al., 2018; Wang et al., 2016.

Stem Cells Proliferation and Differentiation

Stem cells respond well to PBM in terms of proliferation and differentiation.

Not only in the brain: PBM applied to the bone marrow in the legs had a therapeutic effect in a mouse model of Alzheimer's disease.

+ major therapeutic benefits for reducing the infarct area in heart attack models, and in decreasing ischemic kidney injury.

(Arany, 2016; Abrahamse & Hamblin, 2017; Farfara et al., 2015; Blatt et al., 2016; Oron et al., 2014; Kang et al., 2016).

American Journal of Nephrology

Am J Nephrol. 2014;40(5):425-33. doi: 10.1159/000368721. Epub 2014 Nov 18.

Autologous bone-marrow stem cells stimulation reverses post-ischemic-reperfusion kidney injury in rats.

Oron U[1], Tuby H, Maltz L, Sagi-Assif O, Abu-Hamed R, Yaakobi T, Doenyas-Barak K, Efrati S.

Gamma Rhythms

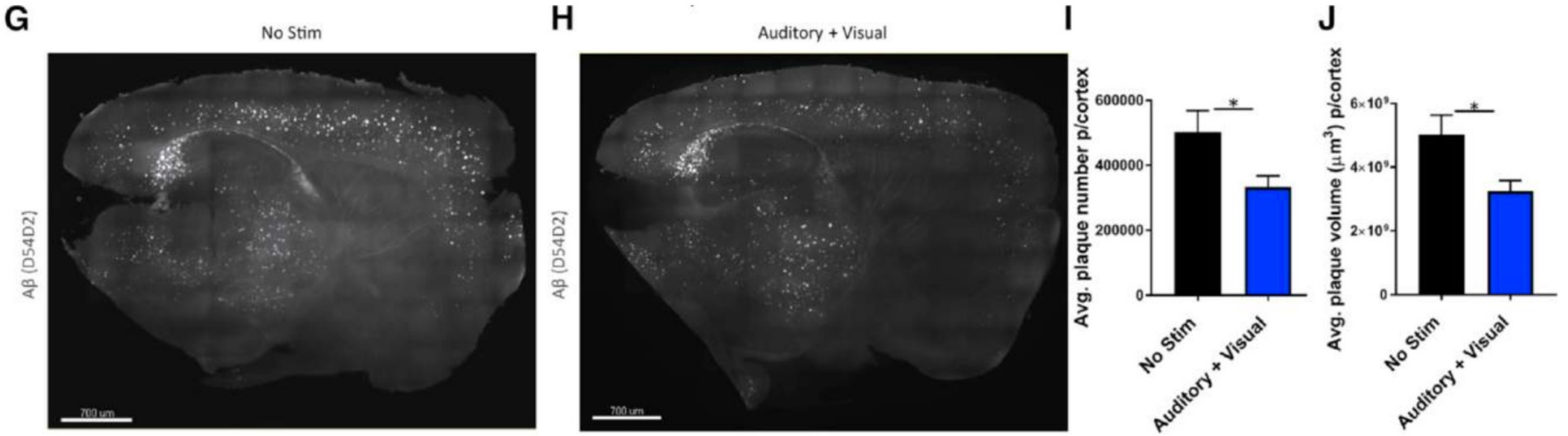
n important series of studies from Dr. Tsai's group at MIT, reported that **40 Hz** pulsed blue light combined with auditory stimulation:

- Reduced the load of amyloid-β peptides in the brain in a mouse model of Alzheimer's Disease;
- Increased neuroprotection and synaptic function;
- Improved cognitive performance.

Li-Huei Tsai, Ph.D.
Picower Institute for
Learning and Memory at MIT

Gamma Rhythms

Auditory + Visual Gamma stimulation in the hippocampus and auditory cortex **reduced Amyloid Levels** in animal models of Alzheimer's disease.



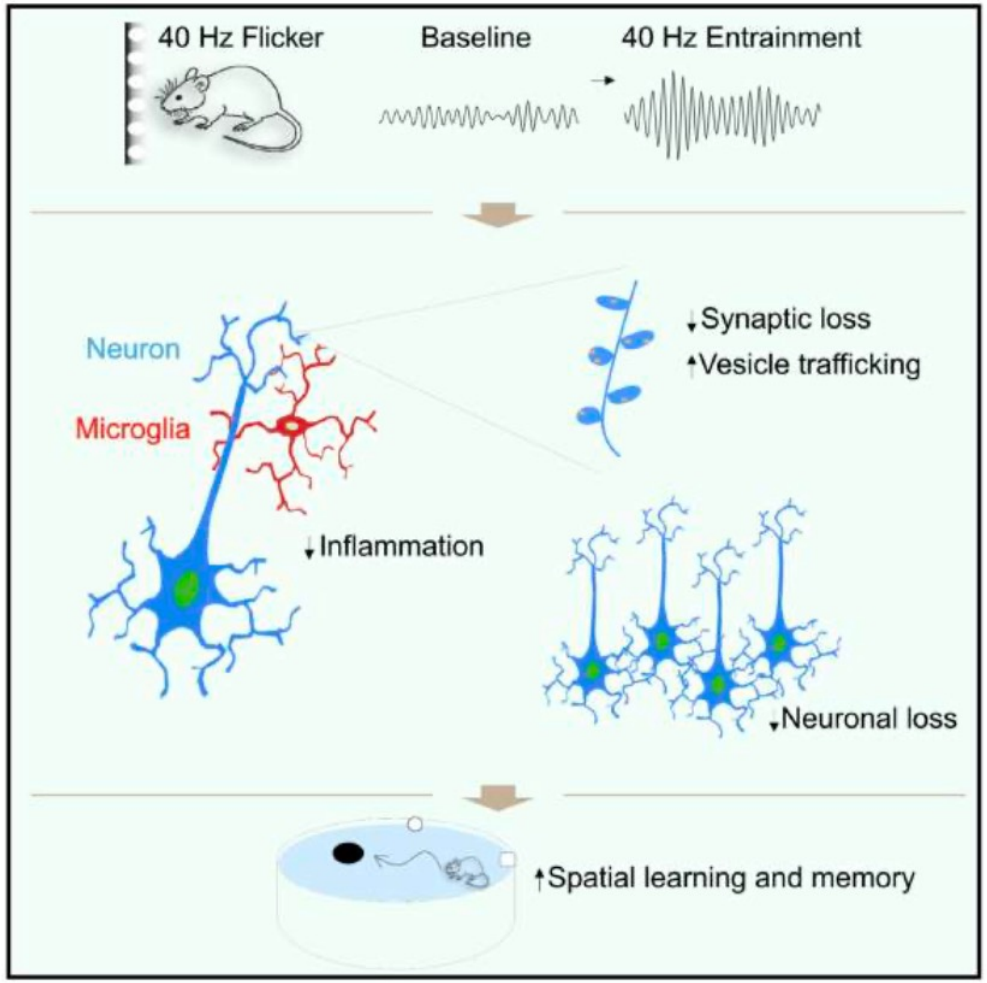
Article

Cell

Multi-sensory Gamma Stimulation Ameliorates Alzheimer's-Associated Pathology and Improves Cognition

Gamma Rhythms

- Reduced synaptic and neuronal loss across multiple brain regions;
- Improved spatial learning and memory.



Adaikkan et al., 2019, Neuron 102, 929–943

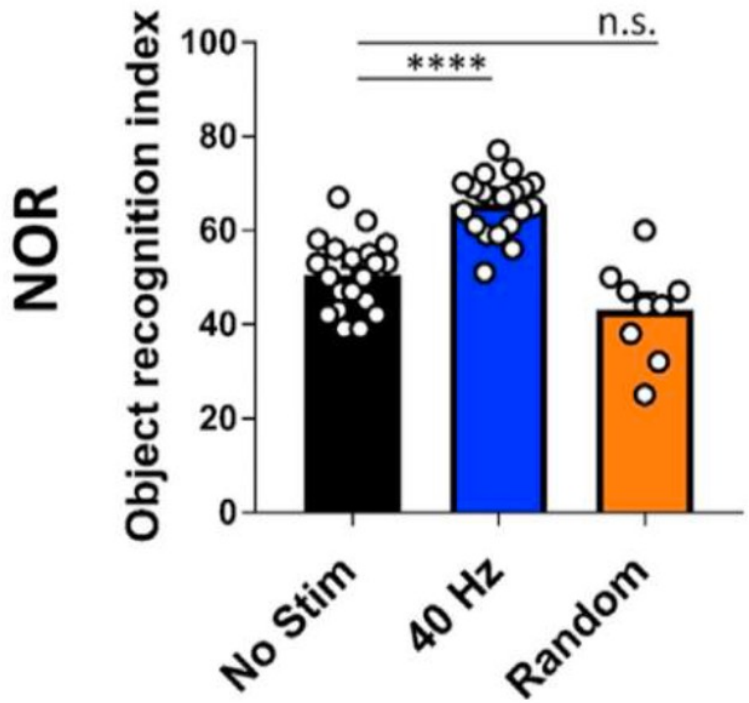
Article

Neuron

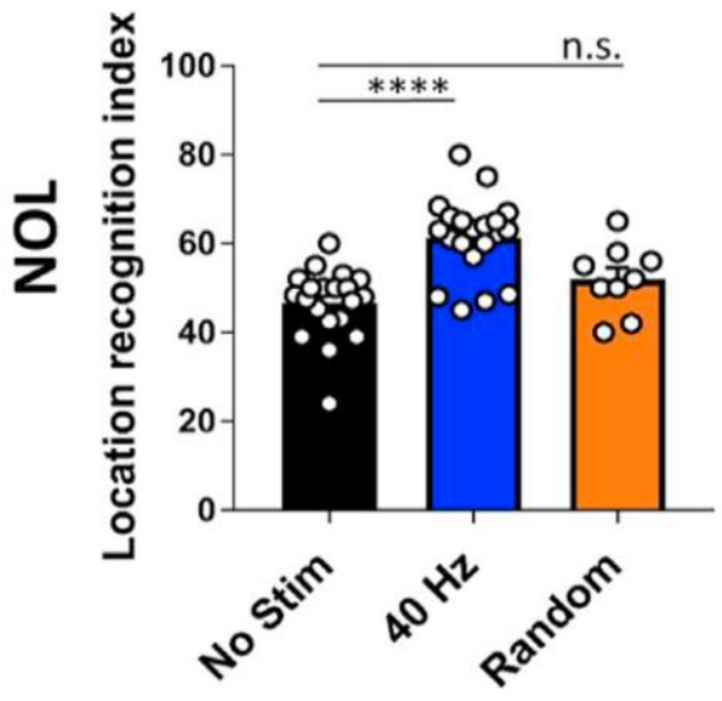
Gamma Entrainment Binds Higher-Order Brain Regions and Offers Neuroprotection

Gamma Rhythms

… Improved memory.



Novel object recognition (NOR)



Novel object location (NOL)

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03

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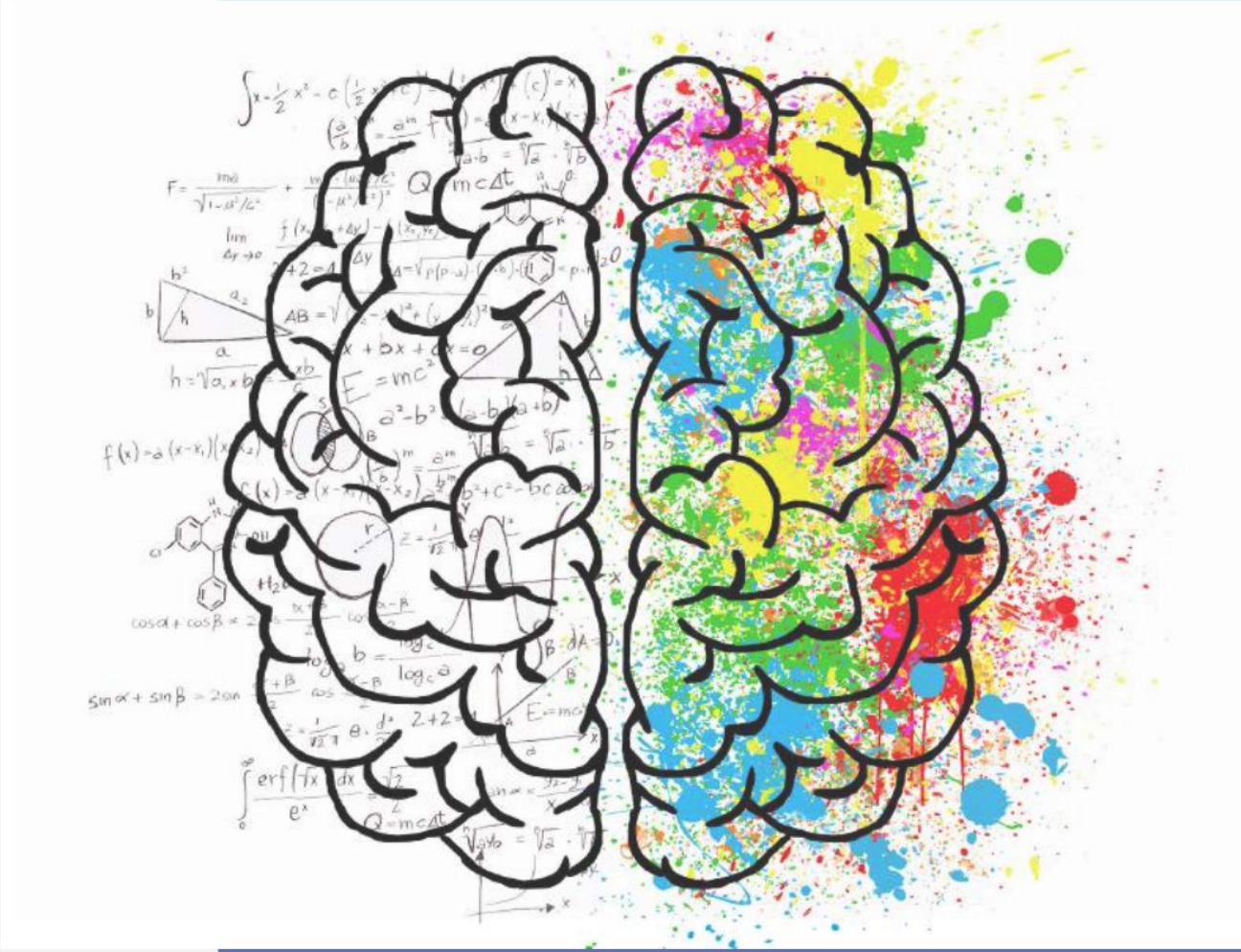

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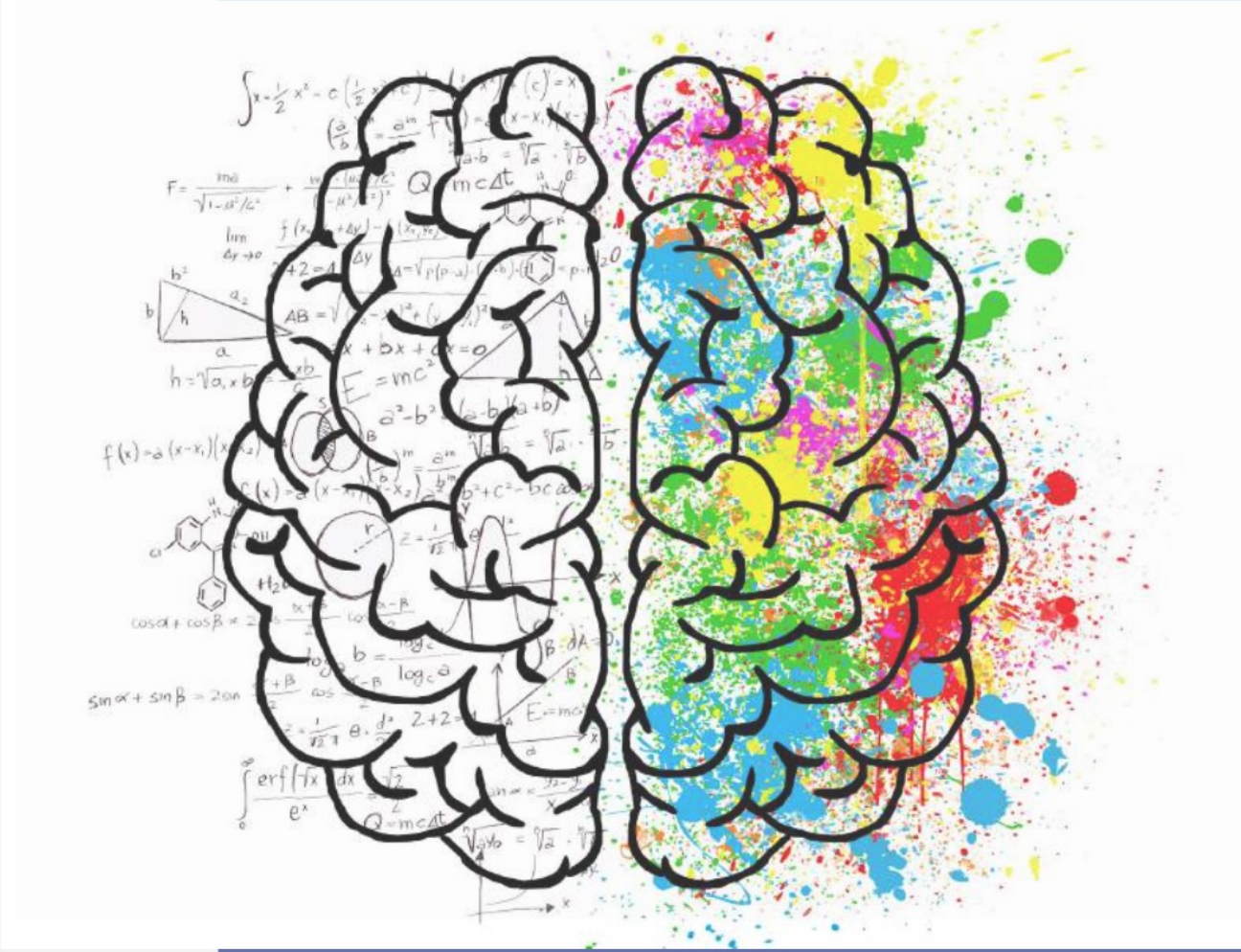


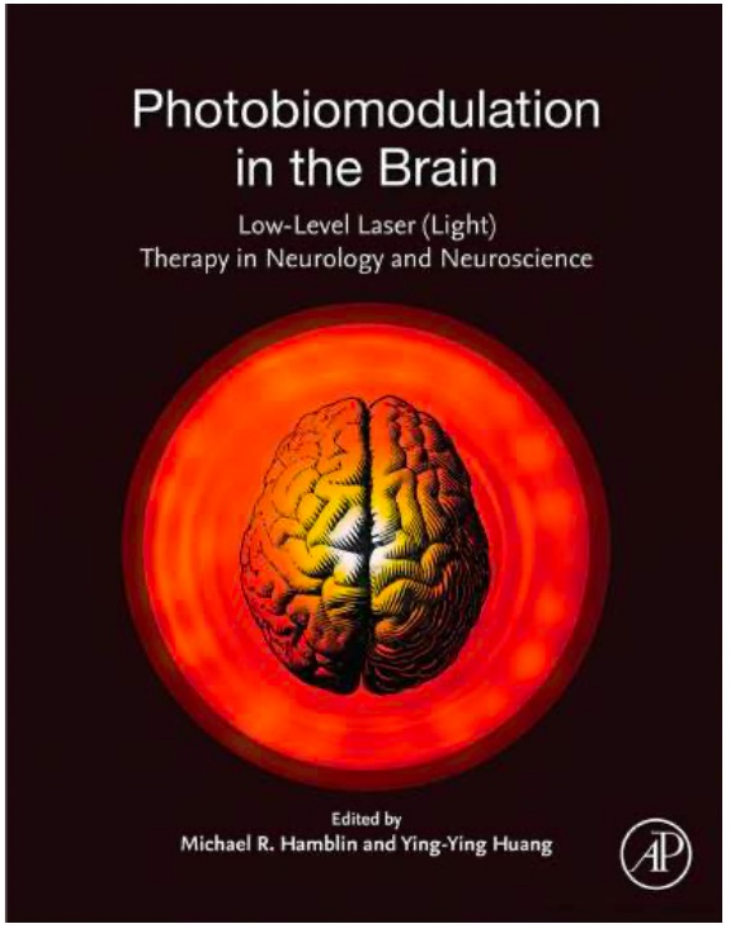
Treatment Protocol

Chapter 34

Cerebral blood flow in the elderly: impact of photobiomodulation

Afonso Shiguemi Inoue Salgado[1,5], Francisco José Cidral-Filho[2,3], Daniel Fernandes Martins[2,3], Ivo I. Kerppers[4] and Rodolfo Borges Parreira[1,5]

[1]Salgado Institute of Integrative Health, Londrina, Brazil, [2]Experimental Neuroscience Laboratory (LaNEx), University of Southern Santa Catarina, Palhocça, Santa Catarina, Brazil, [3]Postgraduate Program in Health Sciences, University of Southern Santa Catarina, Santa Catarina, Brazil, [4]Laboratory of Neuroanatomy and Neurophysiology, University of Centro-Oeste, Guarapuava, Brazil, [5]Residency Program in Integrative Physical Therapy at UNIFIL University, Londrina, Brazil



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HARVARD
UNIVERSITY

tPBM Helmet

Transcranial Photobiomodulation helmet developed with special type of LEDs, for neuro stimulation.

The LEDs irradiate directly to the scalp. Through the hair, for optimum therapeutic outcomes.

For Therapy:

Sit comfortably, put on helmet, and turn on. Sessions last 15 minutes, and device turns off automatically.

Optimal period is between 8pm - 10 pm, as the wave lengths used (IR & RED) stimulate the release of melatonin, which can encourage restful sleep.

2-3 sessions per week.