HHS Public Access

Author manuscript

Mol Neurobiol. Author manuscript; available in PMC 2019 August 01.

Published in final edited form as:

Mol Neurobiol. 2018 August ; 55(8): 6601–6636. doi:10.1007/s12035-017-0852-4.

Brain Photobiomodulation Therapy: A Narrative Review

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Abstract

Brain photobiomodulation (PBM) therapy using red to near-infrared (NIR) light is an innovative treatment for a wide range of neurological and psychological conditions. Red/NIR light is able to stimulate complex IV of the mitochondrial respiratory chain (cytochrome c oxidase) and increase ATP synthesis. Moreover, light absorption by ion channels results in release of Ca^{2+} and leads to activation of transcription factors and gene expression. Brain PBM therapy enhances the metabolic capacity of neurons and stimulates anti-inflammatory, anti-apoptotic, and antioxidant responses, as well as neurogenesis and synaptogenesis. Its therapeutic role in disorders such as dementia and Parkinson's disease, as well as to treat stroke, brain trauma, and depression has gained increasing interest. In the transcranial PBM approach, delivering a sufficient dose to achieve optimal stimulation is challenging due to exponential attenuation of light penetration in tissue. Alternative approaches such as intracranial and intranasal light delivery methods have been suggested to overcome this limitation. This article reviews the state-of-the-art preclinical and clinical evidence regarding the efficacy of brain PBM therapy.

Keywords

photobiomodulation therapy; low-level laser therapy; brain function; cortical neurons; traumatic brain injury; stroke; dementia; depression

Conflict of Interest: The authors declare no conflict of interest.

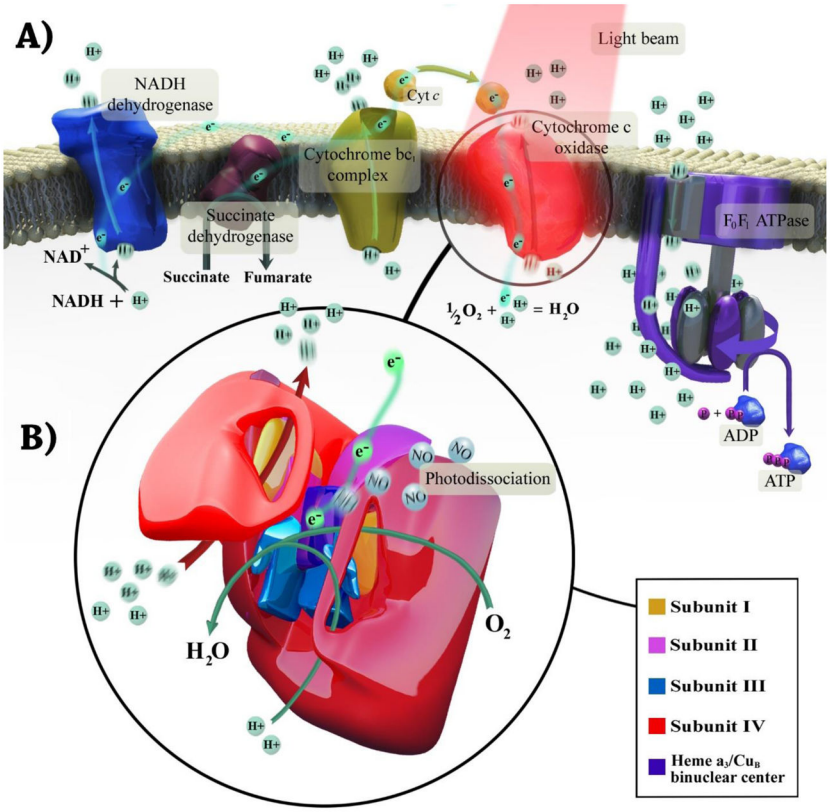

Fig. 1. Mechanism of photobiomodulation therapy in mitochondria

(A) The flow of electrons and protons through the mitochondrial respiratory chain. Photobiomodulation stimulates cytochrome c oxidase, improves its catalytic activity, and elevates ATP synthesis. All these results in enhancement of neuronal respiration and metabolic capacity. (B) The structure of cytochrome c oxidase and electrons path through its subunits. The complex contains two copper centers as well as two heme prosthetic groups. Photobiomodulation may dissociate nitric oxide from binuclear center (a_3/Cu_B), allowing oxygen to return, and facilitates electron transfer and increases proton gradient.

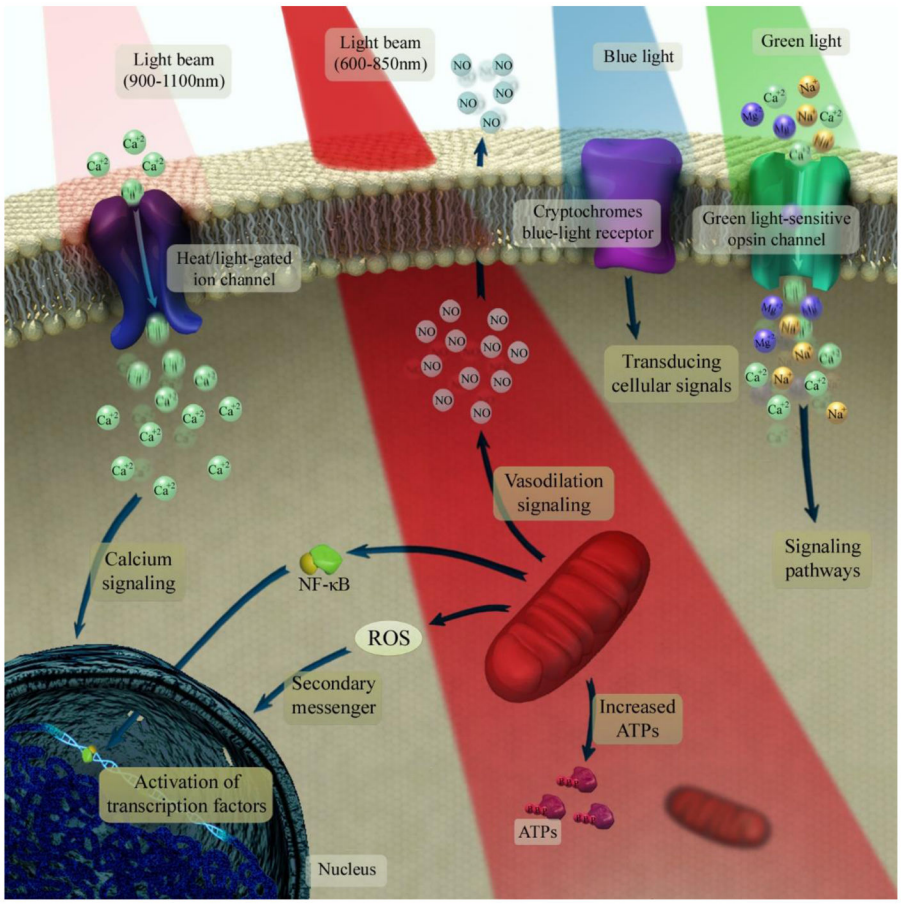

Fig. 2. Photobiomodulation underlying mechanisms at the cellular and molecular levels

Light at 600–850 nm is absorbed by the mitochondrial electron transfer chain and leads to upregulation of the neuronal respiratory capacity. The near-infrared light at range of 900–1100 nm is absorbed by structured water clusters formed in or on a heat/light-gated ion channels. An increase in vibrational energy of water cluster leads to perturb the protein structure and opening the channel which ultimately allows modulation of intracellular Ca^{2+} levels. The absorption of green light by neuronal opsin photoreceptors (OPN2–5) activates transient receptor potential channels which causes non-selective permeabilization to Ca^{2+}, Na^{+} and Mg^{2+}. The cryptochromes (a class of flavoprotein blue-light signaling receptors) absorb blue light and seems to activate the transducing cellular signals via part of the optic nerve to the suprachiasmatic nucleus in the brain, which is important in regulation of the circadian clock.

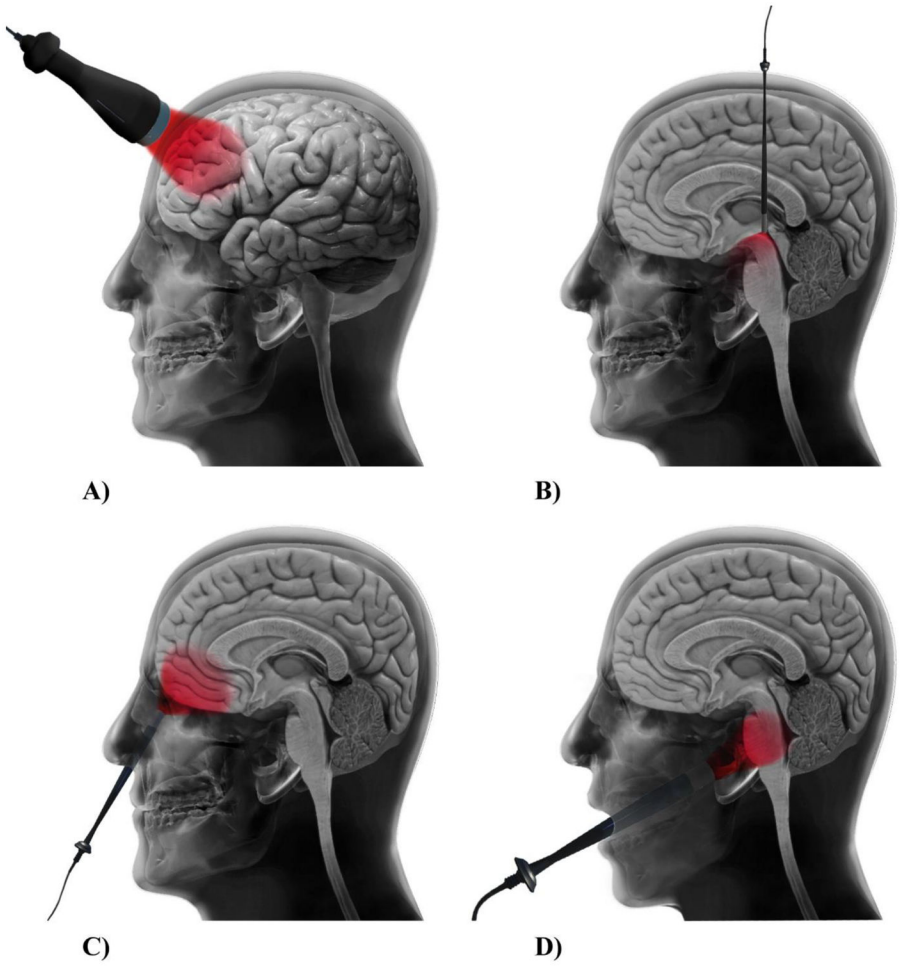

Fig. 3. Different approaches for light delivery to achieve brain photobiomodulation therapy
(A) Transcranial, (B) intracranial, (C) intranasal photobiomodulation therapy, (D) brain photobiomodulation via oral cavity.

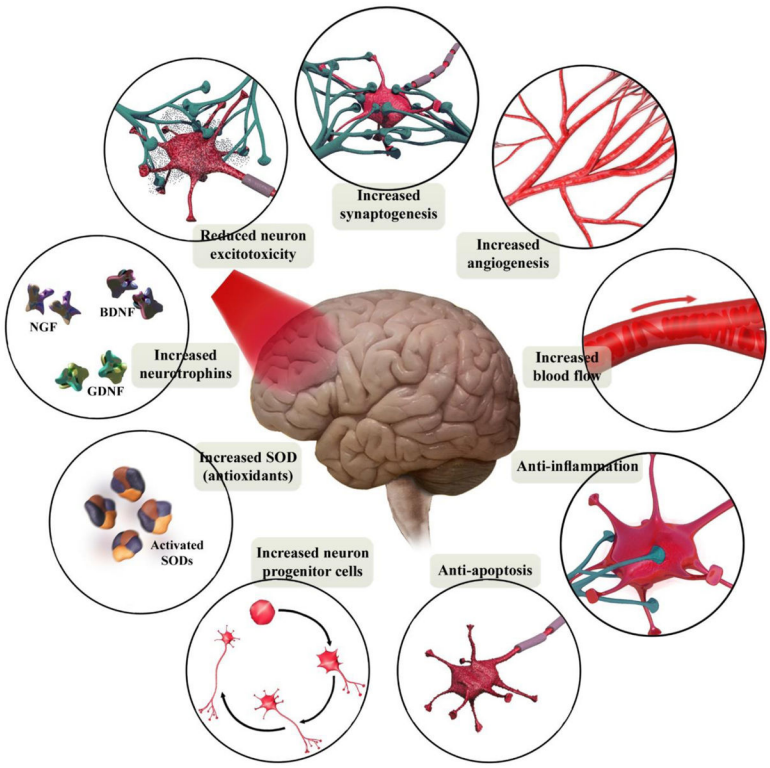

Fig. 4. Brain tissue-specific functional processes that occur after brain photobiomodulation therapy

On a cellular level, photobiomodulation can reduce apoptosis and excitoxicity, increase antioxidants, neurotrophins and stimulate neuroprogenitor cells. On a tissue level, photobiomodulation therapy can increase blood flow and angiogenesis, reduce inflammation and help neurons form new connections. BDNF, brain-derived neurotrophic factor; GDNF, glial-derived neurotrophic factor; NGF, nerve growth factor; SOD, superoxide dismutase.