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REVIEW

Review of transcranial photobiomodulation for major depressive disorder: targeting brain metabolism, inflammation, oxidative stress, and neurogenesis

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Abstract. We examined the use of near-infrared and red radiation (photobiomodulation, PBM) for treating major depressive disorder (MDD). While still experimental, preliminary data on the use of PBM for brain disorders are promising. PBM is low-cost with potential for wide dissemination; further research on PBM is sorely needed. We found clinical and preclinical studies via PubMed search (2015), using the following keywords: "near-infrared radiation," "NIR," "low-level light therapy," "low-level laser therapy," or "LLLT" plus "depression." We chose clinically focused studies and excluded studies involving near-infrared spectroscopy. In addition, we used PubMed to find articles that examine the link between PBM and relevant biological processes including metabolism, inflammation, oxidative stress, and neurogenesis. Studies suggest the processes aforementioned are potentially effective targets for PBM to treat depression. There is also clinical preliminary evidence suggesting the efficacy of PBM in treating MDD, and comorbid anxiety disorders, suicidal ideation, and traumatic brain injury. Based on the data collected to date, PBM appears to be a promising treatment for depression that is safe and well-tolerated. However, large randomized controlled trials are still needed to establish the safety and effectiveness of this new treatment for MDD. [DOI: 10.1117/1.NPh.3.3.031404]

Keywords: near-infrared radiation; photobiomodulation; low-level laser therapy; major depressive disorder; metabolism; inflammation; neurogenesis; oxidative stress; near-infrared; NILT; low-level light therapy.

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1 Introduction

Infrared (IR) light is ubiquitously present to most life on the earth. Of the total amount of solar energy reaching the human skin, 54% is IR and 30% is IR type A—near-infrared—(NIR; with a wavelength range of 760 to 1440 nm),[1] which penetrates through the human skin and reaches deeply into tissue, depending on wavelength and energy.[2]

NIR is used to treat a variety of conditions such as muscle pain,[3] wounds,[4] neuropathic pain,[5] and headache.[6] NIR is also used for wellness and lifestyle purposes such as for cosmetic improvement in peri-orbital wrinkles.[7,8] The clinical use of NIR light applied in NIR-spectroscopy dates from the mid-1980s, when it was used for monitoring of the brain in the neonate and the fetus.[9]

The use of transcranial phototherapy for treating brain disorders started with its application to acute stroke. Numerous preclinical animal studies[10–12] suggested that the application of NIR laser (810 nm) to the head at various times (hours) after induction of an acute stroke had beneficial effects on subsequent neurological performance and reduced lesion size. Evidence was obtained for the anti-inflammatory, anti-apoptotic, and proneurogenesis effects in the brain stimulated by this approach.[13,14] These promising animal studies led to the conduction of a series of clinical trials called NeuroThera Effectiveness and Safety Trials (NEST). All together there were three large studies conducted in 1410 stroke patients [NEST-1 ($n = 120$), NEST-2 ($n = 660$), NEST-3 ($n = 630$)] that demonstrated that NIR light delivered transcranially with a class-IV laser is safe, with no significant differences in rates of adverse events with NIR, when compared to sham exposure.[15–17] Other preclinical studies and clinical trials have suggested that transcranial photobiomodulation (PBM: laser or light emitting diodes—LED) is safe and effective for acute[18–22] and chronic[23–25] traumatic brain injury (TBI) and has beneficial effects on neurodegenerative diseases (Alzheimer's and Parkinson's).[26,27]

For the transcranial treatment of major depressive disorder (MDD), both PBM LEDs and lasers have been experimentally tested, although PBM is not FDA-approved for the treatment of MDD. Certain forms of PBM treatment are also referred to as low-level light therapy (LLLT), since it utilizes light at a low power (0.1 to 0.5 W output at the source) to avoid any heating of tissue. The irradiance of the PBM medical devices (or power density) typically ranges from 1 to 10 times the NIR irradiance from sunlight on the skin (33.6 mW/cm^2 at the zenith).

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