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Review

Photobiomodulation for the aging brain

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Highlights

- Photobiomodulation improves cognitive brain functions during aging in animals and humans.
- Photobiomodulation improves the brain energy metabolism during aging in animals and humans.
- Photobiomodulation alters the neuroinflammatory profile aged animals.

Abstract

Longevity is one of the great triumphs of humanity. Worldwide, the elderly is the fastest growing segment of the population. As a consequence, the number of cases of age-

related cognitive decline and neurological diseases associated with aging, such as Alzheimer's and Parkinson's, has been increasing. Among the non-pharmacological interventions studied for the treatment or prevention of age-related neurocognitive impairment, photobiomodulation (PBM) has gained prominence for its beneficial effects on brain functions relevant to aging brains. In animal models, the neuroprotective and neuromodulatory capacity of PBM has been observed. Studies using both animals and humans have shown promising metabolic and hemodynamic effects of PBM on the brain, such as improved mitochondrial and vascular functions. Studies in humans have shown that PBM can improve electrophysiological activity and cognitive functions such as attention, learning, memory and mood in older people. In this paper we will review the main brain effects of PBM during aging, discuss its mechanisms of action relevant to the aging brain, and call for more controlled studies in older populations.

Introduction

Aging is a multifactorial biological process characterized by a decline in physiological functions (Grady, 2012). Across the world, the number of people aged 60 and over has been growing faster than any other age group. In 2015, the elderly population reached 901 million. Estimates indicate people aged over 60 will reach 1.4 billion by 2030, and 2.1 billion by 2050 (DESA, 2015). This increase in life expectancy may be related to many factors, including changes in the quality of life of the population, greater urbanization, nutritional improvement, increased personal hygiene, better sanitary conditions and adequate work and home environments (Kalache et al., 1987). On the other hand, longevity has been accompanied by an increase in cases of neurological diseases associated with aging, such as late-onset Alzheimer's disease (AD) and Parkinson's disease among others (Mattson and Magnus, 2006).

However, aging is a physiological process not yet fully understood. In recent years, non-pharmacological interventions for the treatment or prevention of age-related brain impairment have been proposed by many researchers (e.g., Gonzalez-Lima et al., 2014; Salgado et al., 2015; De la Torre et al., 2019). Among non-pharmacological interventions, low-level laser therapy or photobiomodulation (PBM) (Anders et al., 2015) has been highlighted for its beneficial brain effects in studies using animals (Rojas and Gonzalez-Lima, 2013; Salehpour et al., 2017; Salehpour et al., 2018b; Cardoso et al., 2021a; Cardoso

et al., 2021b) and humans (Barrett and Gonzalez-Lima, 2013; Vargas et al., 2017; Wang et al., 2017; Saucedo et al., 2021). The hypothesis to explain the beneficial effects of PBM is related to the capacity of brain tissue chromophores to absorb photonic energy, according to the wavelength, and the resulting impact on cell metabolism and brain physiology (Chen et al., 2013; Salehpour et al., 2017; Mitrofanis and Jeffery, 2018). PBM affects cell metabolism in multiple ways. For example, improvement in energy metabolism occurs through mitochondria, by increased oxygen consumption and synthesis of adenosine triphosphate (ATP), altering membrane potential and also promoting an increase in proliferation rates (Hatefi, 1985; Rojas and Gonzalez-Lima, 2011; Rojas et al., 2012; Hamblin, 2016; Cardoso et al., 2021a). There is also evidence that transcranial PBM promotes behavioral changes, such as improved mood, attention, learning and memory, in addition to antidepressant effects (Barrett and Gonzalez-Lima, 2013; Cassano et al., 2016; Vargas et al., 2017; Xu et al., 2017; Salehpour et al., 2017; Cardoso et al., 2021b). In this review we will present some preclinical and clinical evidence highlighting neurobiological and behavioral effects of PBM during brain aging and advocate for the need of more controlled studies.

Section snippets

Mechanisms of action of PBM on the brain

It is already well supported in the literature that the primary mechanism of action of PBM starts with the capacity of cells to absorb photons of red-to-near infrared light (620–1100 nm) by mitochondria photoacceptors. Among these molecules, studies conducted by Tina Karu's research group first identified the mitochondrial enzyme cytochrome c oxidase (CCO) as a fundamental molecule for the beneficial effects of PBM (Karu, 1988; Karu, 1999; Karu et al., 2004; Karu and Kolyakov, 2005). CCO is the …

Light penetration into the brain

Many optical parameters are responsible for light penetration into tissues, such as light scattering, absorption, reflection, refraction, wavelength, energy, power, irradiance, radiant exposure (fluence), exposure time, continuous vs. pulsed wave, fraction protocol, exposed area, distance of the beam source to the target tissue (Rojas and Gonzalez-Lima, 2011; Chung et al., 2012; Henderson and Morries, 2015;Salehpour et al., 2019a). In addition, physiological and anatomical differences and…

Biphasic dose-response effects of PBM

The biphasic dose-response of PBM, also known as hormetic or inverted U-shaped dose-response, is a phenomenon characterized by lower doses that have stimulating effects and higher doses that have inhibitory or even detrimental effects (Rojas et al., 2008; Huang et al., 2009; Rojas and Gonzalez-Lima, 2011; Hamblin, 2016; Salehpour et al., 2018a). Several studies have demonstrated these hormetic effects (Sharma et al., 2011; Rojas et al. 2012). For example, Sharma et al. (2011) irradiated…

Beneficial cognitive effects of PBM on the aging brain

Studies using laboratory animals have shown beneficial cognitive effects of PBM on the aging brain (Michalikova et al., 2008; Salehpour et al., 2017; Salehpour et al., 2018b;Salehpour et al., 2019a). For example, Michalikova et al. (2008) observed that ten days of PBM was able to improve the working memory of CD-1 middle-aged female mice (12 months old) in a 3D maze with a raised arm configuration. However, this study is difficult to evaluate because it provided no information on laser…

Conclusion

Aging is a multifactorial biological process, characterized by a decline in physiological functions, including brain functions. Studies with animals and humans show that PBM can improve cognitive function during this phase of life. It is likely that the ability of PBM to facilitate brain energy and hemodynamic metabolism, reduce inflammatory and oxidative stress levels and regulate the rate of apoptotic proteins is closely related to the beneficial effects on cognitive functions. Moreover,…

Declaration of Competing Interest

The authors declare that they have no conflicts of interest. All authors read and approved the final manuscript.…

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