Received: 2 April 2018 | Accepted: 9 May 2018

DOI: 10.1002/jbio.201800110

Journal of BIOPHOTONICS

FULL ARTICLE

Photobiomodulation induces antinociception, recovers structural aspects and regulates mitochondrial homeostasis in peripheral nerve of diabetic mice

Victória R. da Silva Oliveira[1] | Diego P. Cury[2] | Laura B. Yamashita[1] | Marcos V. Esteca[3] | Ii-Sei Watanabe[2] | Yoko Fee Bergmann[1] | Elaine F. Toniolo[1,4] | Camila S. Dale[1]*

[1]Laboratory of Neuromodulation of Experimental Pain, Department of Anatomy, University of São Paulo, São Paulo, Brazil

[2]Laboratory of Ultrastructure of Cells and Tissues, Department of Anatomy, University of São Paulo, São Paulo, Brazil

[3]Laboratory of Cellular and Tissue Biology, Faculty of Applied Sciences, University of Campinas, Limeira, Brazil

[4]Univeristy City of São Paulo, Medical School, São Paulo, Brazil

***Correspondence**
Camila Squarzoni Dale, Laboratory of Neuromodulation of Experimental Pain, Department of Anatomy, Institute of Biomedical Sciences, University of São Paulo, Av. Prof. Lineu Prestes, 2415, ICB-III, Cidade Universitária, 05508-900 São Paulo, SP, Brazil.
Email: camila.dale@usp.br

Funding information
FAPESP, Grant/Award Numbers: 2014/03270-1, 2015/17136-8, 2016/10372-0

Diabetic peripheral neuropathy (DPN) is a nervous disorder caused by diabetes mellitus, affecting about 50% of patients in clinical medicine. Chronic pain is one of the major and most unpleasant symptoms developed by those patients, and conventional available treatments for the neuropathy, including the associated pain, are still unsatisfactory and benefit only a small number of patients. Photobiomodulation (PBM) has been gaining clinical acceptance once it is able to promote early nerve regeneration resulting in significant improvement in peripheral nerves disabilities. In this work, the effects of PBM (660 nm, 30 mW, 1.6 J/cm^2, 0.28 cm^2, 15 s in a continuous frequency) on treating DPN-induced pain and nerve damage were evaluated in an experimental model of diabetic-neuropathy induced by streptozotocin in mice. PBM-induced antinociception in neuropathic-pain mice was dependent on central opioids release. After 21 consecutive applications, PBM increased nerve growth factor levels and induced structural recovery increasing mitochondrial content and regulating Parkin in the sciatic nerve of DPN-mice. Taking together, these data provide new insights into the mechanisms involved in the effects of PBM-therapy emphasizing its therapeutic potential in the treatment of DPN.

KEYWORDS
diabetic neuropathy, mitochondrial homeostasis, pain, photobiomodulation

1 | INTRODUCTION

Diabetes mellitus is a multifactorial disease characterized by chronic hyperglycemia and dysfunctions in the metabolism. The deficiency in secretion or action of insulin can damage several organs in long term. In extreme cases, in the absence of treatments, ketoacidosis and blood hyperosmolarity can result in coma and death [1].

Peripheral neuropathy is the most common long-term complication in diabetes, being extremely disabling for patients [2]. It is estimated that of the 425 million people affected by diabetes, around 60% to 70% are affected by some form of neuropathy or will develop it at some point in their life [3]. Diabetic peripheral neuropathy (DPN) is a more frequent manifestation, occurring in about 50% of the diabetic patients [4]. Among the symptoms reported by compromised individuals, it also described the appearance of tingling, limb sensitivity loss, weakness and numbness [5], but among them stands out the development of chronic pain, which mainly affects the extremities, manifesting in the form of allodynia and hyperalgesia.

It is known that inadequate glycemic controls, and the duration of diabetes, are directly factors correlated with the development of DPN [6]. However, the mechanisms behind pain emergence remain unclear [4, 7]. Although nerve degeneration (demyelination, and loss of myelinated and

