Treatment Efficacy of Photobiomodulation for Moderate and Advanced Dementia or Alzheimer's Disease: Case Studies

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Abstract

Extensive research is ongoing in the use of photobiomodulation (PBM, often referred to as low level laser therapy) to treat Alzheimer's disease or dementia. The following case studies further confirm that PBM could be a breakthrough approach to limit the progression of this insidious disease. We present four cases, two with mild to moderate dementia and two with more advanced symptoms. Several publications have shown beneficial results, however, several weeks of daily treatments were necessary. The cases described here suggest that moderate or advanced dementia cases can be significantly improved with three or four eight-minute treatments over a 5- 7-day period (MWF).

Key words: Photobiomodulation; Alzheimer's disease; Dementia; Super-pulsed laser; Traumatic Brain Injury (TBI); Laser diode, Case reports

Introduction

In the scientific community there have been multifaceted efforts to find a remedy for Alzheimer's disease and dementia, which so far have consumed billions of US$ in research costs.[1] However one non-pharmaceutical approach called photobiomodulation (PBM) or low-level laser therapy (LLLT) has shown very promising results in some early stage clinical trials and in laboratory animal studies.

PBM involves the delivery of red and/or near-infrared light from a laser or a LED (light emitting diode) to a particular part of the body. PBM can in many circumstances provide physiological benefits lasting much longer than the duration of irradiation. PBM has been widely employed for reducing pain, inflammation, preventing tissue damage, and the stimulation of healing of wounds or other types of injuries.[2] Because PBM/LLLT does not involve any drugs or invasive modalities, it is remarkably free of side effects, and has been generally recognized as safe by the FDA.

One of the most impressive applications of PBM has been its use to treat a variety of brain disorders.[3,4] These disorders have included acute[5] or chronic [6,7] traumatic brain injury, acute stroke,[8] a variety of psychiatric disorders[9,] Parkinson's disease[10] and Alzheimer's disease or dementia.[11,12].

The protocol described by Saltmarche et al[13] for dementia patients included treatment with a combination of transcranial and intranasal LED devices, which are used daily at home for a 12-week period. We have obtained the same results with four eight-minute treatments delivered over a seven-day period.

We use a high-powered super-pulsed laser with 905 nm and 660 nm diodes. Most other researchers use LEDs in their treatment. (see figure 1) We have utilized this device for treatment in our clinical practice for over 15 years with no adverse effects reported by any patients or families. This system was originally FDA cleared for pain management and we initially treated chronic pain, orthopedic trauma, sports injury and arthritis. After treating hundreds of patients over the years with no adverse effects, we started treating simple headaches, migraines and concussions. After a short time, based on the patients reporting clinical benefits, it was concluded that the near infrared laser must be penetrating through the skull plate! LEDs have significantly less power and usually are incorporated in a helmet. Previously the protocol is for the patient to wear this helmet for half an hour every day for approximately 12 weeks. However, improvements have been made reducing the time to six minutes per day for 28 days. The patients we treated with the laser experienced significant improvement in 3-4 treatments in most cases.

Our first publication in 2012 described the efficacy of super - pulsed 905 nm low level laser therapy in the management of traumatic brain injury (TBI) in one case study.[14] Despite repeated efforts having been undertaken to present our findings to the Department of Defense or the National Football League, it fell on "deaf ears". Our most recent papers described the clinical improvement in patients treated with our laser system for Post-traumatic Stress Disorder (PTSD) as well as for mild dementia[15,16] We have also recently obtained positive results in a case study of children and adults with attention deficit hyperactivity disorder (ADHD) (submitted for publication).

Methods

The Theralase® TLC-2000 CLT laser head we used contained five superpulsed 905 nm diodes (200 nsec pulse duration) each with the ability to put out 200 mW average power, plus four 660 nm diodes each with the ability to put out 100 mW power. (see figure 1.) Patients were treated on a MWF schedule (i.e. three times) over a five-day period. Six areas were treated for three minutes each, four areas on the pre-frontal cortex and two areas on the mid-brain. Power settings were 100 mW for each of the 905 nm diodes and 75 mW for the 660 nm diodes. The energy delivered per site was 144 J, and the total energy delivered over six sites was 864 J. The patient was put in a supine position and protective eyewear was worn. No discomfort was reported by any patient. Moderate cases were given the Mini Mental State Exam, but advanced cases did not have the ability to respond.

Figure 1. Theralase TLC 2000. Toronto, Canada

Figure 2. Patient being treated for Alzheimer's utilizing Theralase TLC 1000 super- pulsed laser

Case: 1 Moderate Dementia

A 92-year-old female presented with memory loss, low energy and was becoming very argumentative, a trait not previously displayed. The first treatment was preceded by a short interview. She was very lucid and even had a sense of humor. After the treatment, we spoke to the daughter she lives with and said "I don't think we can help her as there seems to be nothing wrong with her." The daughter requested we continue to administer additional treatments. Prior to the second treatment, the daughter informed the authors that the patient had asked her daughter for a hot fudge sundae, her favorite dessert that she had not asked for in three months! We administered a total of four treatments and the following testimonial letter was written 3 months after the last treatment.

"Mr. Banas provided 4 treatments for my 94-year-old mother to assist her with beginning stage dementia. After the first treatment, I noticed she was not sleeping as much during the day. As the treatment progressed, I also noted she requested a hot fudge sundae, her favorite, which she has not done in more than a year. She also became more alert during the day; previously had been sleeping most of the day, getting up at my urging to drink ensure, water, and have a light meal of eggs, or toast and soup. While her memory short term is not different, she has more alertness, and interacts more with me as she had previous to her decline. Also noted, she wanted to go out to lunch, a favorite pastime which she had been loath to do lately. We prepared to go to lunch, as she is on oxygen 24/7 and uses a cane or walker to get around. I came to help her get her coat on and she had her lipstick out and was putting it on her lips. I asked about it and she said, since we're going out I thought I should put some make up on but couldn't find anything but lipstick. My mother had for years worn lipstick and would reapply it after having anything to eat or drink. Her lips were 'addicted' to lipstick! I was quite surprised and pleased to see her using it as this was something she stopped several years ago. She has also started to watch some of her old favorite television shows, another thing she had stopped. She is napping during the day, but more like long ago when she would get up and watch the news and have her coffee and breakfast, watch another show and then nap after lunch. Mr. Banas felt that the changes were a result of the increased blood flow from the light therapy treatments to her brain. I can't argue with that as it was the only thing that changed and I did note several improvements. My mom is not argumentative at all and has always had a positive outlook to life, but these changes have improved her quality of life. Thank you!"

Case 2. Mild to moderate dementia.

A former 84 year-old AFL professional football player was diagnosed with mild to moderate dementia five years previously. His wife had died before onset and his children were not proactive in an effort to help curb further onset (i.e. puzzles, games etc.) However, he was still very functional at this point in time but slow in responding to normal everyday day activities. Four treatments were administered over an 8 day period. The children reported that he no longer needed excessive day time naps and his energy level was significantly increased. He would respond more quickly when asked a question. One of his close teammates came to visit after a one-year hiatus and he was not recognized immediately. However, the old teammate continued to engage his old friend about old times he did recall some stories. However, when the treatment was given a day prior to the Super Bowl, he could not remember the game was the next day even though it was mentioned twice during the session with him.

Case 3: Advanced dementia

This advanced case involved a 72-year-old man presented to us by his wife as a last resort. He had incontinence issues and could not follow directions. Using the standard protocols, we started to see remarkable results after the third treatment. For instance, when we told him to get up on the table he was able to do this properly without direction. In addition, when asked to open the goggle case and put the glasses on which he did with little effort, which he was not able to do previously. His incontinence issues were no longer a problem. Most encouragingly, after arriving for a treatment I walked out to greet them at the car to see how he would respond. He saw me coming and he turned to his wife and informed her, that I was coming out to greet them; This was tremendously gratifying.

Unfortunately, after the 4th treatment the family observed some adverse effects. He displayed excessive energy and some aggressive tendencies. He no longer would sleep through the night. At one point, in the middle of the night he got up and was rearranging furniture in the living room. His wife asked him what he was doing and he told her to "mind her own business!" We had to temporarily cut back on the treatments and in addition, stopped treating the prefrontal cortex. As of this writing, this patient is still doing well and he has not had a maintenance treatment for 6 weeks. His wife is getting the sleep she needed. He controls his urinary issues but is wearing Depends for his defecation. He is apologetic to the wife for this issue.

Case 4: Advanced Dementia

The 82-year-old mother of an alternative medicine physician asked me if I could help his mom. She had been diagnosed with dementia 7 years previously and needed a caretaker full time. Since I was only in the area for a short time I told him I did not think I could help her unless perhaps there was an anger management problem. He reported there was and the issue had only manifested itself in the last year. He had the caretaker bring her to the clinic for a single treatment. Twenty minutes after the treatment, the caregiver and mother were in the recovery room. The mother was Cuban and could not speak English. I asked her 40-year-old niece if she had experienced anything from the single treatment expecting nothing of significance. To the surprise of both of us, upon seeing her right her right after the treatment "…she smiled and gave me a hug something she had not done for the 6 months we have been together! "

Conclusion

Published studies from multiple institutions are reporting significant benefits from photobiomodulation treatment in Alzheimer's disease or dementia. A group including Berman and Huang has described a helmet with 1100 LEDs emitting 1060–1080 nm light pulsed at 10 Hz with a 50% duty cycle.[17] PBM was administered for 6 minutes daily over 28 consecutive days in a pilot trial of 11 patients. A non-significant improvement was seen in the active compared to the placebo group with respect to MME and ADAS-Cog scores. The same group then went on to recruit a much larger group of fifty-seven patients.[18] Significant improvements were seen in the active group with respect to MMSE, Logical Memory Tests I and II, Trail Making Tests A and B, Boston Naming Test, and Auditory Verbal Learning Tests. A further analysis revealed no difference between the responses of male and female patients[19]Additional case studies have reported the benefits in Alzheimer's disease patients using PBM alone[20], or PBM combined with a ketogenic diet.[21]

The mechanism of action of PBM on the brain is multifactorial in nature, and several biochemical and cellular processes have been proposed to be responsible for the beneficial effects as shown in Figure 2. (3). Theorized mechanisms of action include: (a) Stimulation of mitochondria by photons and the consequent increase in cytochrome c oxidase activity and intracellular adenosine triphosphate (ATP).[22] (b) Improvement in regional blood flow and oxygen delivery to the brain parenchyma by triggering nitric oxide (NO) production.[23] (c) Anti-inflammatory effects caused by changing the phenotype of the brain microglia from pro-inflammatory M1 to anti-inflammatory M2.[24] This switch results from changing the mitochondrial metabolism from glycolysis towards oxidative phosphorylation by light absorption. It should be noted that M2 microglia can carry out phagocytosis, and could therefore dispose of beta-amyloid plaque in the brains of Alzheimer's patients.[25] (d) Anti-apoptotic affects caused by PBM, which could prevent the death of cortical neurons.[26] (e) Stimulation of neurogenesis (production of new neurons from progenitor cells existing in the brain), and synaptogenesis (production of new connections between existing neurons)[27]. (f) Balancing of connections between intrinsic brain networks in the brain (especially the default mode network.[28]

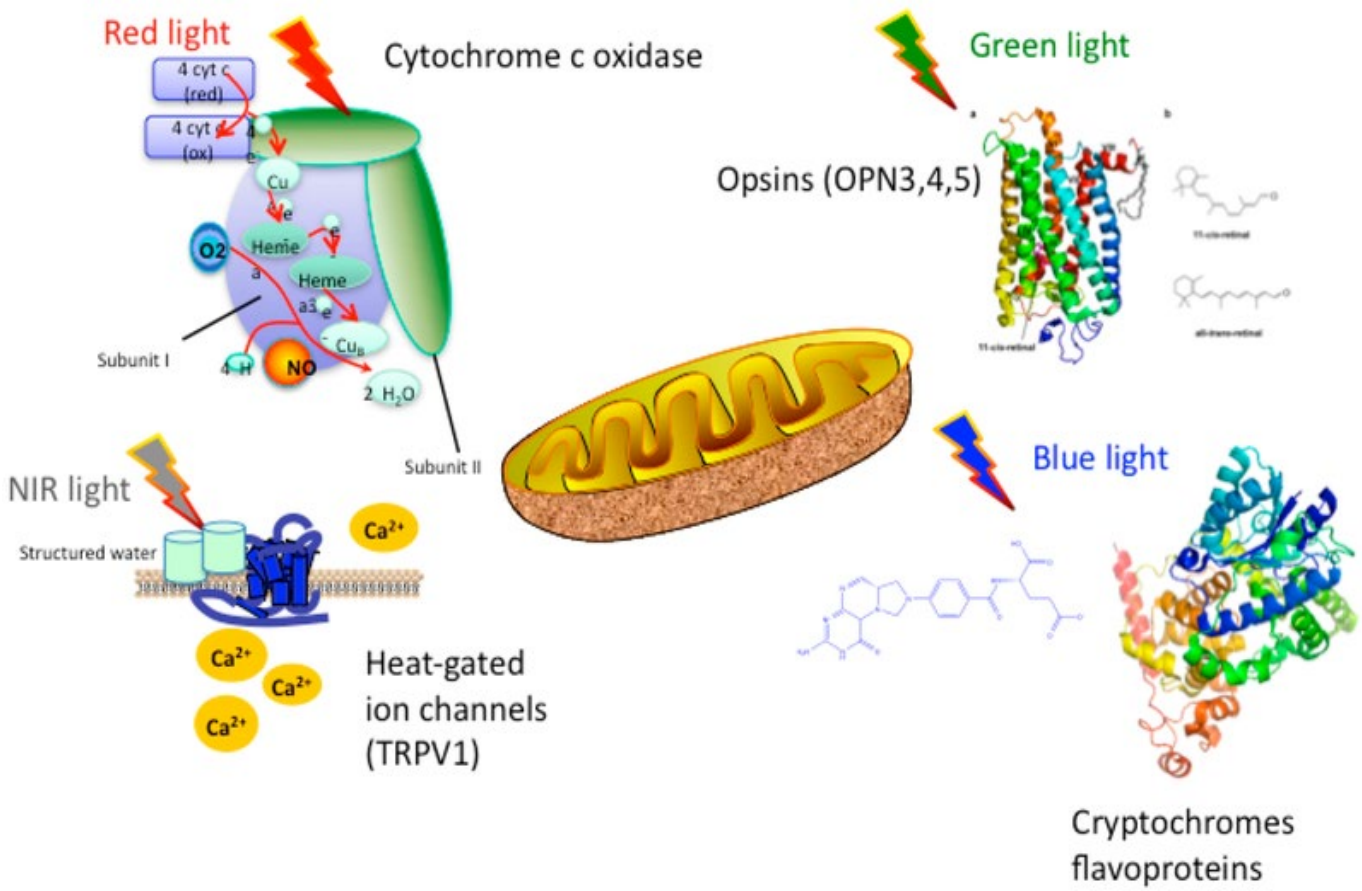

Figure 3. Proposed chromophores for PBM that can absorb different wavelengths of light. It should be noted that there is considerable overlap between the chromophores, and that the NIR absorbed by structured water is likely to be longer wavelength (>950 nm).

The rapidly increasing number of reports of the benefits of PBM for Alzheimer's disease and dementia suggest that this non-invasive, non-pharmaceutical, and safe treatment approach should be more widely adopted. Although LED helmets are attractive options, it is possible that higher-power super-pulsed lasers could provide improvements in a shorter period of time, and could be used by therapists as an in-office treatment. The growing amount of data concerning the cellular and molecular mechanisms of action provides a scientific basis for its wider adoption.

References

1. Prados MJ, Liu Y, Jun H, Lam J, Mattke S. Projecting the long-term societal value of a disease-modifying treatment for Alzheimer's disease in the United States. Alzheimer's & Dementia. 2022;18(1):142-51.
2. Hamblin MR, Agrawal T, de Sousa MV. Handbook of Low-Level Laser Therapy. Boca Raton, FL, USA: CRC Press; 2016.

3. Hamblin MR. Shining light on the head: Photobiomodulation for brain disorders. BBA Clin. 2016;6:113-24.
4. Hamblin MR, Huang YY. Photobiomodulation in the Brain: Low-Level Laser (Light) Therapy in Neurology and Neuroscience. Amsterdam, Netherlands: Academic Press; 2019.
5. Figueiro Longo MG, Tan CO, Chan S-t, Welt J, Avesta A, Ratai E, et al. Effect of Transcranial Low-Level Light Therapy vs Sham Therapy Among Patients With Moderate Traumatic Brain Injury. JAMA Network Open. 2020;3(9):e2017337.
6. Naeser MA, Martin PI, Ho MD, Krengel MH, Bogdanova Y, Knight JA, et al. Transcranial, Red/Near-Infrared Light-Emitting Diode Therapy to Improve Cognition in Chronic Traumatic Brain Injury. Photomed Laser Surg. 2016;34(12):610-26.
7. Naeser MA, Saltmarche A, Krengel MH, Hamblin MR, Knight JA. Improved cognitive function after transcranial, light-emitting diode treatments in chronic, traumatic brain injury: two case reports. Photomed Laser Surg. 2011;29(5):351-8.
8. Naeser MA, Hamblin MR. Potential for transcranial laser or LED therapy to treat stroke, traumatic brain injury, and neurodegenerative disease. Photomed Laser Surg. 2011;29(7):443-6.
9. Salehpour F, Gholipour-Khalili S, Farajdokht F, Kamari F, Walski T, Hamblin MR, et al. Therapeutic potential of intranasal photobiomodulation therapy for neurological and neuropsychiatric disorders: a narrative review. Reviews in the Neurosciences. 2020;31(3):269-86.
10. Liebert A, Bicknell B, Laakso EL, Hller G, Jalilitabaei P, Tilley S, et al. Improvements in clinical signs of Parkinson's disease using photobiomodulation: a prospective proof-of-concept study. BMC Neurology. 2021;21(1).
11. Hamblin MR. Photobiomodulation for Alzheimer's Disease: Has the Light Dawned? Photonics. 2019;6(3).
12. Hamblin MR, Salehpour F. Photobiomodulation of the Brain: Shining Light on Alzheimer's and Other Neuropathological Diseases. Journal of Alzheimer's Disease. 2021:1-3.
13. Saltmarche AE, Naeser MA, Ho KF, Hamblin MR, Lim L. Significant Improvement in Cognition in Mild to Moderately Severe Dementia Cases Treated with Transcranial Plus Intranasal Photobiomodulation: Case Series Report. Photomed Laser Surg. 2017;35(8):432-41.
14. Stephan W, Banas LJ, Bennett M, Tunceroglu H. Efficacy of super-pulsed 905 nm Low Level Laser Therapy (LLLT) in the management of Traumatic Brain Injury (TBI): A case study. World Journal of Neuroscience. 2012;02(04):231-3.
15. Lamartiniere R, Bergeron R, Aung-Din R, Bennett M, Stephan W, Banas L. Photobiomodulation treatment for brain disorders: posttraumatic stress disorder (PTSD) and dementia In: Hamblin MR, Huang YY, editors. Photobiomodulation in the Brain: Low-Level Laser (Light) Therapy in Neurology and Neuroscience. Amsterdam, Netherlands: Academic Press; 2019.

16. Stephan W, Din R, Banas L, Thomas J, Kochert C, Lamartiniere R, et al. Management of Post-Traumatic Stress (PTSD) Dementia and Other Neuro-Degenerative Disease with Photo-Medicine: Clinical Experience and Case Studies. Open Journal of Psychiatry. 2017;7:386-94.
17. Berman MH, Halper JP, Nichols TW, Jarrett H, Lundy A, Huang JH. Photobiomodulation with Near Infrared Light Helmet in a Pilot, Placebo Controlled Clinical Trial in Dementia Patients Testing Memory and Cognition. J Neurol Neurosci. 2017;8:176.
18. Huang JH, Stevens AB, Yi SS, Wu E, Dayawansa S, Dougal G, et al. Transcranial Near Infrared Light Stimulations Improve Cognition in Patients with Dementia. Aging and disease. 2021;12(4):954.
19. Qi X, Nizamutdinov D, Berman MH, Dougal G, Chazot PL, Wu E, et al. Gender Differences of Dementia in Response to Intensive Self-Administered Transcranial and Intraocular Near-Infrared Stimulation. Cureus. 2021.
20. Salehpour F, Hamblin MR, DiDuro JO. Rapid Reversal of Cognitive Decline, Olfactory Dysfunction, and Quality of Life Using Multi-Modality Photobiomodulation Therapy: Case Report. Photobiomodul Photomed Laser Surg. 2019;37(3):159-67.
21. Horner S, Berger L, Gibas K. Nutritional Ketosis and photobiomodulation remediate mitochondria warding off Alzheimer's disease in a diabetic, ApoE4+ patient with mild cognitive impairment: A case report. Photodiagnosis and Photodynamic Therapy. 2020;30:101777.
22. Cardoso FdS, Barrett DW, Wade Z, Gomes da Silva S, Gonzalez-Lima F. Photobiomodulation of Cytochrome c Oxidase by Chronic Transcranial Laser in Young and Aged Brains. Frontiers in Neuroscience. 2022;16.
23. Baik JS, Lee TY, Kim NG, Pak K, Ko S-H, Min JH, et al. Effects of Photobiomodulation on Changes in Cognitive Function and Regional Cerebral Blood Flow in Patients with Mild Cognitive Impairment: A Pilot Uncontrolled Trial. Journal of Alzheimer's Disease. 2021;83(4):1513-9. 8
24. Yang L, Tucker D, Dong Y, Wu C, Lu Y, Li Y, et al. Photobiomodulation therapy promotes neurogenesis by improving post-stroke local microenvironment and stimulating neuroprogenitor cells. Experimental Neurology. 2018;299:86-96.
25. Singer AC, Martorell AJ, Douglas JM, Abdurrob F, Attokaren MK, Tipton J, et al. Noninvasive 40-Hz light flicker to recruit microglia and reduce amyloid beta load. Nature Protocols. 2018;13(8):1850-68.
26. Davies DJ, Hadis M, Di Pietro V, Lazzarino G, Forcione M, Harris G, et al. Photobiomodulation reduces hippocampal apoptotic cell death and produces a Raman spectroscopic "signature". Plos One. 2022;17(3):e0264533.
27. Xuan W, Vatansever F, Huang L, Hamblin MR. Transcranial low-level laser therapy enhances learning, memory, and neuroprogenitor cells after traumatic brain injury in mice. J Biomed Opt. 2014;19(10):108003.
28. Xuan W, Agrawal T, Huang L, Gupta GK, Hamblin MR. Low-level laser therapy for traumatic brain injury in mice increases brain derived neurotrophic factor (BDNF) and synaptogenesis. J Biophotonics. 2015;8(6):502-11.