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Transcranial Photobiomodulation-Therapy: Scientific Mechanisms, Studies and The Weber Medical Infrared Helmet

A presentation by
Martin Junggebauer, M.Sc.

Contents

Transcranial Low-Level-Laser-Therapy

Martin Junggebauer, M.Sc.

- 2013: Graduation as M.Sc. International Development Economics & Global Health
- Since 2013: Collaboration with WeberMedical: Business Development and Research
- Since 2013: Co-founder and co-president of ISLA Research Group - a non-profit scientific organization that conducts in-vivo-research in the area of antimicrobial photodynamic therapy.
- 2015: Co-author of the book “Low-Level-Laser-Therapy: Foundations and Clinical Applications”.
- Since 2019: Founder and CEO of J-MedTech-Consulting: Consulting agency for clinic set ups, distribution of other technologies in the sector of integrative medicine.
- Since January 2022: **Student of “Post-Graduate Diploma in Neuroscience and Psychology of Mental Health” at King´s College London**

Mechanisms of Action

Transcranial Low-Level Laser Therapy

Basics

Transcranial Low-Level Laser Therapy (TLLLT) is the direct irradiation of the human brain with highly focused infrared lasers.

Unlike other wavelengths, infrared light has the ability to penetrate bones and to bring light energy to the targeted brain areas.

Light energy is absorbed by different types of cells to trigger a broad range of intra-cellular effects.

LED therapy is non-invasive, painless and non-thermal.

Why infrared light?

The optimum wavelength for max. skull penetration is between 805 nm and 830 nm (infrared).

Studies show that the light reaches a depth of 4-5 cm past skull (or 3 cm into brain tissue)

Mechanisms

How PBM affects cellular activity in the brain

Stimulation of the mitochondrial respiratory chain (cytochrome c oxidase) → Increases ATP production

Release of NO by photodissociation vasodilatory effects →
- Improves lymphatic flow = Increased cerebral blood flow
- Activation of beneficial cellular pathways

Brief increase in reactive oxygen species → Stimulates cytoprotective, anti-oxidant, anti- inflammatory, and anti-apoptotic effects in cells

Improved oxygen availability and oxygen consumption

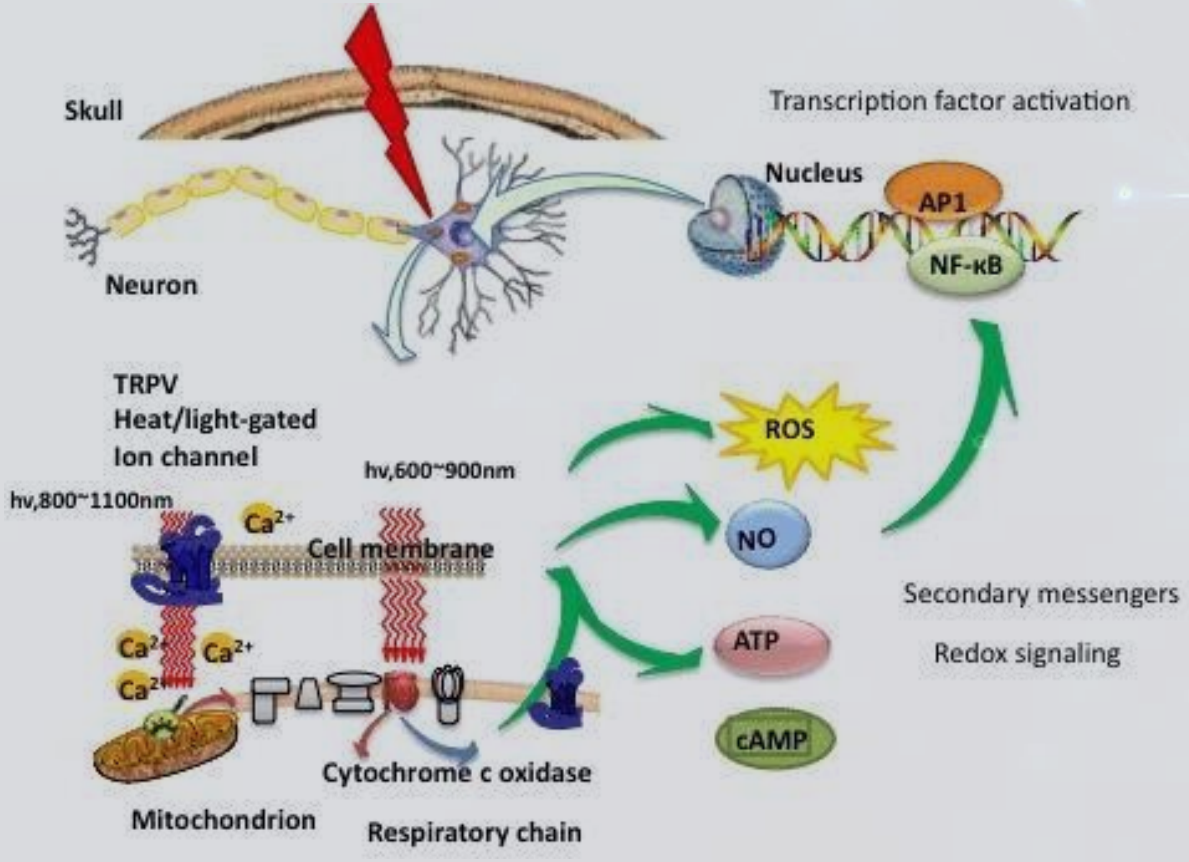
Activation of signaling pathways and transcription factors that cause long-lasting changes in protein expression

Mechanisms

The important role of molecular photoreceptors

Molecular and intracellular mechanisms of transcranial low-level laser (light) or photobiomodulation

Michael R. Hamblin, Shining light on the head: Photobiomodulation for brain disorders, BBA Clinical (2016)



Cytochrome c oxidase and **heat-gated ion channels** are two of the most important molecular photoreceptors or chromophores inside neuronal cells. They absorb photons that penetrate into the brain.

The signaling pathways and activation of transcription factors lead to the eventual effects of PBM in the brain.

AP1 = activator protein 1

ATP = adenosine triphosphate

Ca2+ = calcium ions

cAMP = cyclic adenosine monophosphate

NF-kB = nuclear factor kappa B

NO = nitric oxide

ROS = reactive oxygen species

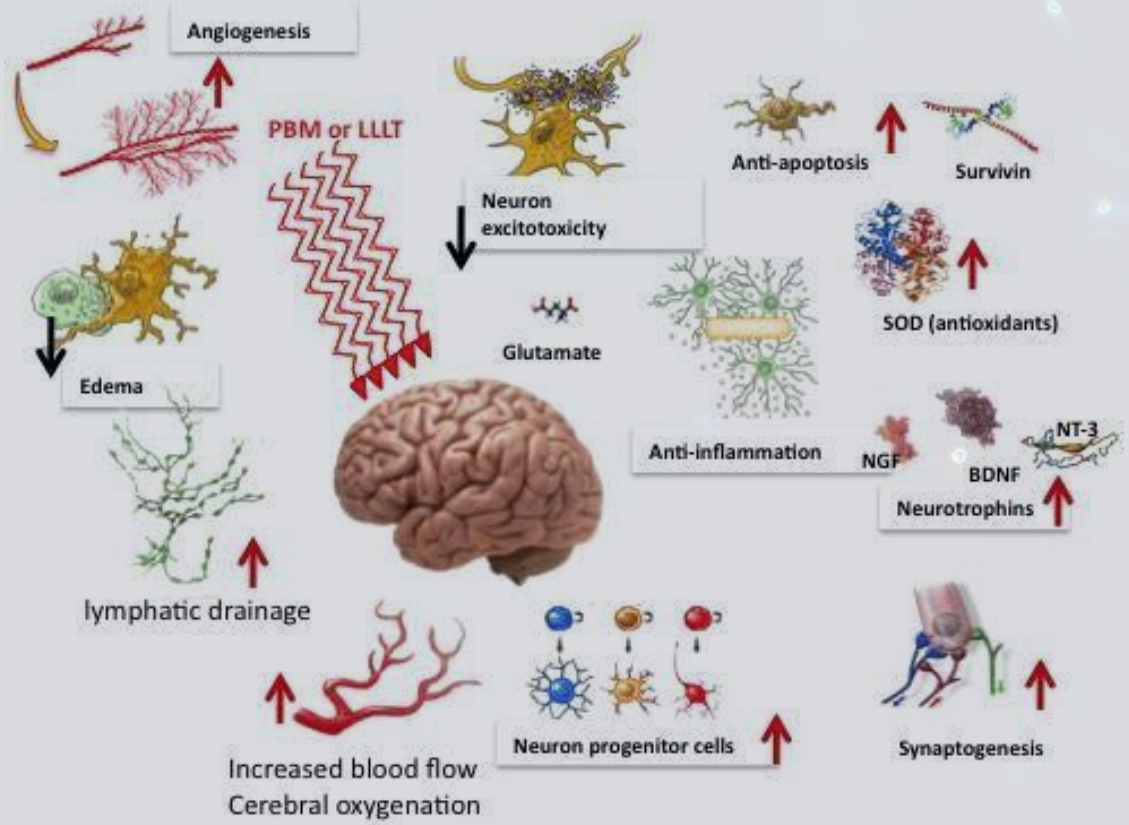
TRPV = transient receptor potential vanilloid

Mechanisms

How PBM benefits brain disorders

Tissue specific processes that occur after PBM and benefit a range of brain disorders

Michael R. Hamblin, Shining light on the head: Photobiomodulation for brain disorders, BBA Clinical (2016)



Summary: The most important effects

- Increase of ATP production = improved brain metabolism
- Improved cerebral blood flow and lymphatic flow
- Improved cerebral oxygenation
- Reduction of neuroinflammation
- Improved neuronal signaling
- Increased neurogenesis and synaptogenesis
- Anti-apoptotic proteins
- Anti-oxidant effects

Neurodegenerative Diseases

Impaired brain energetics is involved in the cause and progression of NDAs

Review > Nat Rev Drug Discov. 2020 Sep;19(9):609-633. doi: 10.1038/s41573-020-0072-x.
Epub 2020 Jul 24.

Brain energy rescue: an emerging therapeutic concept for neurodegenerative disorders of ageing

The brain requires a continuous supply of energy in the form of ATP, most of which is produced from glucose by oxidative phosphorylation in mitochondria, complemented by aerobic glycolysis in the cytoplasm. When glucose levels are limited, ketone bodies generated in the liver and lactate derived from exercising skeletal muscle can also become important energy substrates for the brain. In neurodegenerative disorders of ageing, brain glucose metabolism deteriorates in a progressive, region-specific and disease-specific manner - a problem that is best characterized in Alzheimer disease, where it begins presymptomatically. This Review discusses the status and prospects of therapeutic strategies for countering neurodegenerative disorders of ageing by improving, preserving or rescuing brain energetics. The approaches described include restoring oxidative phosphorylation and glycolysis, increasing insulin sensitivity, correcting mitochondrial dysfunction, ketone-based interventions, acting via hormones that modulate cerebral energetics, RNA therapeutics and complementary multimodal lifestyle changes.

Neurodegenerative Diseases:

Alzheimer´s / Dementia

J Alzheimers Dis. 2021;83(4):1431-1452. doi: 10.3233/JAD-210029.

Photobiomodulation Therapy for Dementia: A Systematic Review of Pre-Clinical and Clinical Studies

Farzad Salehpour [1] [2], Mahsa Khademi [3], Michael R Hamblin [4]

Methods: Literature was searched between 1967 and 2020 using a range of keywords relevant to PBM and dementia. The light source and wavelength(s), output power, irradiance, irradiation time, fluence or total energy (dose), operation mode (continuous or pulsed) irradiation, approach and site, number of treatment sessions, as well as study outcome(s) were extracted.

Results: Out of 10,473 initial articles, 36 studies met the inclusion criteria. Nine articles reported in vitro studies, 17 articles reported studies in animal models of dementia, and 10 studies were conducted in dementia patients. All of the included studies reported positive results. The clinical studies were limited by the small number of patients, lack of placebo controls in some instances, and only a few used objective neuroimaging methods.

Conclusion: The preliminary evidence of clinical benefit, the lack of any adverse effects, and the remarkable ease of use, suggest larger clinical trials should be conducted as soon as possible.

TLLLT for Alzheimer's Disease

General Study Results

Daniel M.Johnstone, CécileMoro, JonathanStone1, Alim-LouisBenabid, J.Mitrofanis:

TABLE 1 | Studies reporting on NIr treatment in Alzheimer's disease.

Findings with NIr application	Study	Model	Species
↑ Cell survival ↑ ATP content ↓ β-amyloid aggregates	Sommer et al., 2012	*In vitro* (neuroblastoma cells internalized with β-amyloid)	Human cells
↓ β-amyloid plaques ↓ Oxidative stress ↓ hyperphosphorylated tau	Purushothuman et al., 2014, 2015	APP/PS1, K3691 transgenics (chronic)	Mouse
↓ β-amyloid plaques ↓ Inflammation ↑ ATP content ↑ Mitochondrial function	DeTaboada et al., 2011	APP transgenic (chronic)	Mouse
↓ β-amyloid plaques ↓ Oxidative stress ↓ Hyperphosphorylated tau ↑ Heat shock proteins	Grillo et al., 2013	TASTPM transgenic (chronic)	Mouse
↑ Cognitive behavioral deficits	Michalikova et al., 2008 DeTaboada et al., 2011	CD1 transgenic (acute) APP transgenic (chronic)	Mouse

Human studies: Alzheimer´s

2017

Photomed Laser Surg. 2017 Aug;35(8):432-441. doi: 10.1089/pho.2016.4227. Epub 2017 Feb 10.

Significant Improvement in Cognition in Mild to Moderately Severe Dementia Cases Treated with Transcranial Plus Intranasal Photobiomodulation: Case Series Report

Anita E Saltmarche [1], Margaret A Naeser [2 3], Kai Fai Ho [4], Michael R Hamblin [5 6], Lew Lim [7]

Materials and methods: The study used 810 nm, 10 Hz pulsed, light-emitting diode devices combining transcranial plus intranasal PBM to treat the cortical nodes of the DMN (bilateral mesial prefrontal cortex, precuneus/posterior cingulate cortex, angular gyrus, and hippocampus). Five patients with mild to moderately severe cognitive impairment were entered into 12 weeks of active treatment as well as a follow-up no-treatment, 4-week period. Patients were assessed with the MMSE and Alzheimer's Disease Assessment Scale (ADAS-cog) tests. The protocol involved weekly, in-clinic use of a transcranial-intranasal PBM device; and daily at-home use of an intranasal-only device.

Results: There was significant improvement after 12 weeks of PBM (MMSE, $p < 0.003$; ADAS-cog, $p < 0.023$). Increased function, better sleep, fewer angry outbursts, less anxiety, and wandering were reported post-PBM. There were no negative side effects. Precipitous declines were observed during the follow-up no-treatment, 4-week period. This is the first completed PBM case series to report significant, cognitive improvement in mild to moderately severe dementia and possible AD cases.

Conclusions: Results suggest that larger, controlled studies are warranted. PBM shows potential for home treatment of patients with dementia and AD.

Human studies: Alzheimer´s

2019

Randomized Controlled Trial > Photobiomodul Photomed Laser Surg. 2019 Mar;37(3):133-141.
doi: 10.1089/photob.2018.4555. Epub 2019 Feb 13.

Effects of Home Photobiomodulation Treatments on Cognitive and Behavioral Function, Cerebral Perfusion, and Resting-State Functional Connectivity in Patients with Dementia: A Pilot Trial

Linda L Chao [1 2 3]

(NIR) PBM therapy. ***Materials and methods:*** Eight participants (mean age: 79.8 ± 5.8 years old) diagnosed with dementia by their physicians were randomized to 12 weeks of usual care (UC, $n = 4$) or home PBM treatments ($n = 4$). The NIR PBM treatments were administered by a study partner at home three times per week with the Vielight Neuro Gamma device. The participants were assessed with the Alzheimer's Disease Assessment Scale-cognitive (ADAS-cog) subscale and the Neuropsychiatric Inventory (NPI) at baseline and 6 and 12 weeks, and with arterial spin-labeled perfusion magnetic resonance imaging (MRI) and resting-state functional MRI at baseline and 12 weeks. ***Results:*** At baseline, the UC and PBM groups did not differ demographically or clinically. However, after 12 weeks, there were improvements in ADAS-cog (group × time interaction: $F_{1,6} = 16.35$, $p = 0.007$) and NPI (group × time interaction: $F_{1,6} = 7.52$, $p = 0.03$), increased cerebral perfusion (group × time interaction: $F_{1,6} = 8.46$, $p < 0.03$), and increased connectivity between the posterior cingulate cortex and lateral parietal nodes within the default-mode network in the PBM group. ***Conclusions:*** Because PBM was well tolerated and associated with no adverse side effects, these results support the potential of PBM therapy as a viable home treatment for individuals with dementia.

Human studies: Alzheimer´s

2021

Aging Dis. 2021 Jul; 12(4): 954–963.
Published online 2021 Jul 1. doi: 10.14336/AD.2021.0229
PMCID: PMC8219492
PMID: 34221541

Transcranial Near Infrared Light Stimulations Improve Cognition in Patients with Dementia

Damir Nizamutdinov,[1,2] Xiaoming Qi,[1] Marvin H Berman,[3] Gordon Dougal,[4] Samantha Dayawansa,[1,2] Erxi Wu,[1,2,5,6] S. Stephen Yi,[6] Alan B Stevens,[1] and Jason H Huang[1,2,*]

with an active photobiomodulation for 6 min twice daily during 8 consequent weeks. Sham treatment consisted of same treatment routine with a sham device. Neuropsychological battery was obtained before and after treatment. Analysis of variance (ANOVA) was used to analyze outcomes. Sixty subjects were enrolled. Fifty-seven subjects completed the study and had not reported health or adverse side effects during or after the treatment. Three subjects dropped out from trial for health issues unrelated to use of tNIR light treatment. Treatment with active device resulted in improvements of cognitive functions and changes were: an average increase of MMSE by 4.8 points; Logical Memory Tests I and II by ~3.0 points; Trail Making Tests A and B by ~24%; Boston Naming Test by ~9%; improvement of both Auditory Verbal Learning Tests in all subtest categories and overall time of performance. Many patients reported improved sleep after ~7 days of treatment. Caregivers noted that patients had less anxiety, improved mood, energy, and positive daily routine after ~14-21 days of treatment. The tNIR light treatments demonstrated safety and positive cognitive improvements in patients with dementia. Developed treatment protocol can be conveniently used at home. This study suggests that additional dementia treatment trials are warranted with a focus on mitigating caregivers' burden with tNIR light treatment of dementia patients.

Neurodegenerative Diseases:

Parkinson´s Disease

TLLLT for Parkinson's Disease

General Study Results

Daniel M.Johnstone, CécileMoro, JonathanStone1, Alim-LouisBenabid, J.Mitrofanis:

TABLE 2 | Studies reporting on NIr treatment in Parkinson's disease.

Findings with NIr application	Study	Model	Species
↑ Cell survival (striatal and cortical cells) ↑ ATP content ↓ Oxidative stress	Liang et al., 2008; Ying et al., 2008	*In vitro* (rotenone, MPTP)	Rat cells
↑ Mitochondrial function ↓ Oxidative stress	Quirk et al., 2012b	*In vitro* (neuroblastoma cells overexpressing <-synuclein)	Human cells
↑ mitochondrial movement	Trimmer et al., 2009	*In vitro* (hybrid cells with mitochondrial DNA from Parkinson's disease patients)	Human cells
↑ Cell survival (TH^+ cells)	Shaw et al., 2010	MPTP (acute)	Mouse
↑ Cell survival (TH^+ cells)	Peoples et al., 2012	MPTP (chronic)	
↑ Cell survival (TH^+ cells)	Purushothuman et al., 2013	K369I transgenic (chronic)	
↑ Cell survival (TH^+ cells)	Moro et al., 2013, 2014; Johnstone et al., 2014b	MPTP (acute)	
↑ Cell survival (TH^+ cells)	El Massri et al., 2015	MPTP (acute, sub-chronic)	
↑ Cell survival (TH^+ cells)	Reinhart et al., 2015b	MPTP (acute)	
↑ Cell survival (TH^+ cells)	Reinhart et al., 2015a	6OHDA hemi-parkinsonian	Rat
↑ Cell survival (TH^+ and Nissl-stained cells)	Darlot et al., 2015	MPTP (sub-acute)	Monkey
↓ Oxidative stress ↓ Hyperphosphorylated tau	Purushothuman et al., 2013	K369I transgenic (chronic)	Mouse
↑ Flight ↑ Complex IV-dependent respiration ↓ Mutant mitochondria defects	Vos et al., 2013	pink1 mutant	Flies
↓ Abnormal basal ganglia activity (Fos immunoreactivity)	Shaw et al., 2012	MPTP (acute)	Mouse
↑ Locomotive behavior	Whelan et al., 2008	MPTP (acute)	Mouse
	Desmet et al., 2009	MPTP (acute)	
	Quirk et al., 2012b	A53T(<-synuclein transgenic)	
	Moro et al., 2013; Reinhart et al., 2015b	MPTP (acute)	
↓ Apomorphine-induced rotations	Reinhart et al., 2015a	6OHDA hemi-parkinsonian	Rat
↑ Locomotive behavior, clinical signs	Darlot et al., 2015	MPTP (sub-acute)	Monkey
↓ Clinical signs	Zhao et al., 2003; Maloney et al., 2010; Burchman, 2011	Parkinson's patients	Human
	Quietmind Foundation trial (http://www.youtube.com/watch?v=9X-hjgay7pg)		

Human studies: Parkinson´s

2019

› Photobiomodul Photomed Laser Surg. 2019 Oct;37(10):615-622. doi: 10.1089/photob.2019.4663. Epub 2019 Sep 19.

"Buckets": Early Observations on the Use of Red and Infrared Light Helmets in Parkinson's Disease Patients

Catherine L Hamilton [1], Hala El Khoury [1], David Hamilton [1], Frank Nicklason [1 2], John Mitrofanis [1]

Background: Parkinson's disease is a well-known neurological disorder with distinct motor signs and non-motor symptoms. ***Objective:*** We report on six patients with Parkinson's disease that used in-house built photobiomodulation (PBM) helmets. ***Methods:*** We used "buckets" lined with light-emitting diodes (LEDs) of wavelengths across the red to near-infrared range (i.e., 670, 810, and 850 nm; *n* = 5) or an homemade intranasal LED device (660 nm; *n* = 1). Progress was assessed by the patients themselves, their spouse, or their attending medical practitioners. ***Results:*** We found that 55% of the initial signs and symptoms of the six patients showed overall improvement, whereas 43% stayed the same and only 2% got worse. We also found that PBM did not target a specific sign or symptom, with both motor and nonmotor ones being affected, depending on the patient. ***Conclusions:*** In summary, our early observations are the first to note the impact of PBM on patients' signs and symptoms over an extended period, up to 24 months, and lays the groundwork for further development to clinical trial.

Human studies: Parkinson´s

2021

Randomized Controlled Trial. BMC Neurol. 2021 Jul 2;21(1):256.
doi: 10.1186/s12883-021-02248-y.

Improvements in clinical signs of Parkinson's disease using photobiomodulation: a prospective proof-of-concept study

Methods: Twelve participants with idiopathic PD were recruited. Six were randomly chosen to begin 12 weeks of transcranial, intranasal, neck and abdominal PBM. The remaining 6 were waitlisted for 14 weeks before commencing the same treatment. After the 12-week treatment period, all participants were supplied with PBM devices to continue home treatment. Participants were assessed for mobility, fine motor skills, balance and cognition before treatment began, after 4 weeks of treatment, after 12 weeks of treatment and the end of the home treatment period. A Wilcoxon Signed Ranks test was used to assess treatment effectiveness at a significance level of 5%.

Results: Measures of mobility, cognition, dynamic balance and fine motor skill were significantly improved ($p < 0.05$) with PBM treatment for 12 weeks and up to one year. Many individual improvements were above the minimal clinically important difference, the threshold judged to be meaningful for participants. Individual improvements varied but many continued for up to one year with sustained home treatment. There was a demonstrable Hawthorne Effect that was below the treatment effect. No side effects of the treatment were observed.

Conclusions: PBM was shown to be a safe and potentially effective treatment for a range of clinical signs and symptoms of PD. Improvements were maintained for as long as treatment continued, for up to one year in a neurodegenerative disease where decline is typically expected. Home treatment of PD by the person themselves or with the help of a carer might be an effective therapy option. The results of this study indicate that a large RCT is warranted.

Parameters

810 nm		
-		
posterior	anterior	nasal
3	1	1
100 mW	75 mW	25mW
40 Hz	40 Hz	40 Hz
~1 cm	~1 cm	~1 cm
100 mW/cm^2	75 mW/cm^2	25 mW/cm^2
400 mW		
2100 s		
2100 s		
60 J	45 J	15 J
3	1	1
180 J	45 J	15 J
3 x per week for 4 weeks		
2 x per week for 4 weeks		
1 x per week for 4 weeks		
3 x per week for 25 or 40 weeks		

Animal models: PBM Mechanisms in PD

2019

Biomolecules. 2020 Apr 15;10(4):610. doi: 10.3390/biom10040610.

Photobiomodulation for Parkinson's Disease in Animal Models: A Systematic Review

Farzad Salehpour [1 2 3], Michael R Hamblin [4 5]

The Model

Use of compounds that damage the mitochondria.

Although the animal models of PD do not completely mimic the human disease, they have been useful for studying the pathophysiology of PD, and for testing the effectiveness of novel treatments, including DBS and PBM.

Take-ways

Evidence suggests that transcranial PBM could act via the cytochrome-C-oxidase target of near infrared light, to increase ATP and influence downstream cellular signalling to reduce oxidative stress and neuroinflammation and to upregulate synaptogenesis and neurogenesis.

The two most popular frequencies are 10 Hz (the so-called alpha rhythm) and 40 Hz (the so-called gamma rhythm).

As PD in humans is a chronic degenerative disease, it is expected that PBM therapy would need to be continued for the foreseeable future.

TLLLT for Parkinson's Disease

General Study Results

Case study: 10 weeks of Transcranial LLLT on a Parkinson's patient

YouTube https://www.youtube.com/watch?v=9X-hjgay7pg

Psychological and Mental Disorders

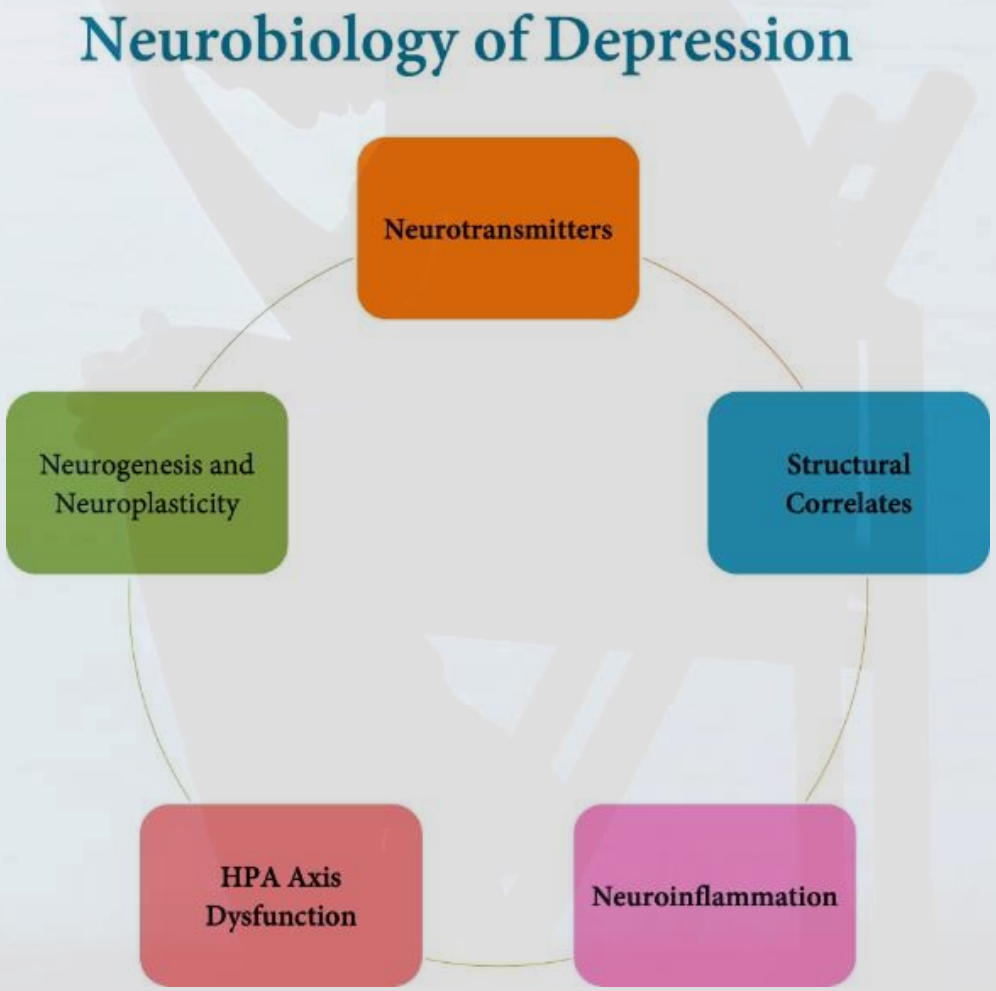
Psychological and Mental Disorders: Major Depressive Disorder (MDD)

Background: Neurobiology of Depression

The root causes of depression are much more complex than stated by the monoamine hypothesis. They can be conceptualized in a matrix of genetic, epigenetic and environmental factors that influence processing biases, belief formation and stress reactivity.

On the mechanical level, various pathophysiological mechanisms are at play. Together they can be summarized as the **Neurobiology of Depression**.

T-LLLT specifically targets neuroinflammations, impaired neurogenesis, oxidative stress, hypometabolism, and decreased cerebral blood flow.



Human studies: T-LLLT for MDD

2009

Behav Brain Funct. 2009 Dec 8;5:46. doi: 10.1186/1744-9081-5-46.

Psychological benefits 2 and 4 weeks after a single treatment with near infrared light to the forehead: a pilot study of 10 patients with major depression and anxiety

Results: At 2-weeks post treatment 6 of 10 patients had a remission (a score </= 10) on the HAM-D and 7 of 10 achieved this on the HAM-A. Patients experienced highly significant reductions in both HAM-D and HAM-A scores following treatment, with the greatest reductions occurring at 2 weeks. Mean rCBF across hemispheres increased from 0.011 units in the off condition to 0.043 units in the on condition, for a difference of 0.032 (95% CI: -0.016, 0.080) units, though this result did not reach statistical significance. Immediately after treatment the PANAS improved to a significantly greater extent with NIR "on" relative to NIR "off" when a hemisphere with more positive HEV was treated than when one with more negative HEV was treated. We observed no side effects.

Conclusion: This small feasibility study suggests that NIR-PBM may have utility for the treatment of depression and other psychiatric disorders and that double blind randomized placebo-controlled trials are indicated.

Human studies: T-LLLT for MDD

2018

Photomed Laser Surg. 2018 Dec;36(12):634-646. doi: 10.1089/pho.2018.4490. Epub 2018 Oct 20.

Transcranial Photobiomodulation for the Treatment of Major Depressive Disorder. The ELATED-2 Pilot Trial

Objective: Our objective was to test the antidepressant effect of transcranial photobiomodulation (t-PBM) with near-infrared (NIR) light in subjects suffering from major depressive disorder (MDD). ***Background:*** t-PBM with NIR light is a new treatment for MDD. NIR light is absorbed by mitochondria; it boosts cerebral metabolism, promotes neuroplasticity, and modulates endogenous opioids, while decreasing inflammation and oxidative stress. ***Materials and methods:*** We conducted a double-blind, sham-controlled study on the safety and efficacy [change in Hamilton Depression Rating Scale (HAM-D_{17}) total score at end-point] of adjunct t-PBM NIR [823 nm; continuous wave (CW); 28.7 × 2 cm^2; 36.2 mW/cm^2; up to 65.2 J/cm^2; 20-30 min/session], delivered to dorsolateral prefrontal cortex, bilaterally and simultaneously, twice a week, for 8 weeks, in subjects with MDD. Baseline observation carried forward (BOCF), last observation carried forward (LOCF), and completers analyses were performed. ***Results:*** The effect size for the antidepressant effect of t-PBM, based on change in HAM-D_{17} total score at end-point, was 0.90, 0.75, and 1.5 (Cohen's *d*), respectively for BOCF (n = 21), LOCF (n = 19), and completers (n = 13). Further, t-PBM was fairly well tolerated, with no serious adverse events. ***Conclusions:*** t-PBM with NIR light demonstrated antidepressant properties with a medium to large effect size in patients with MDD. Replication is warranted, especially in consideration of the small sample size.

Human studies: T-LLLT for MDD

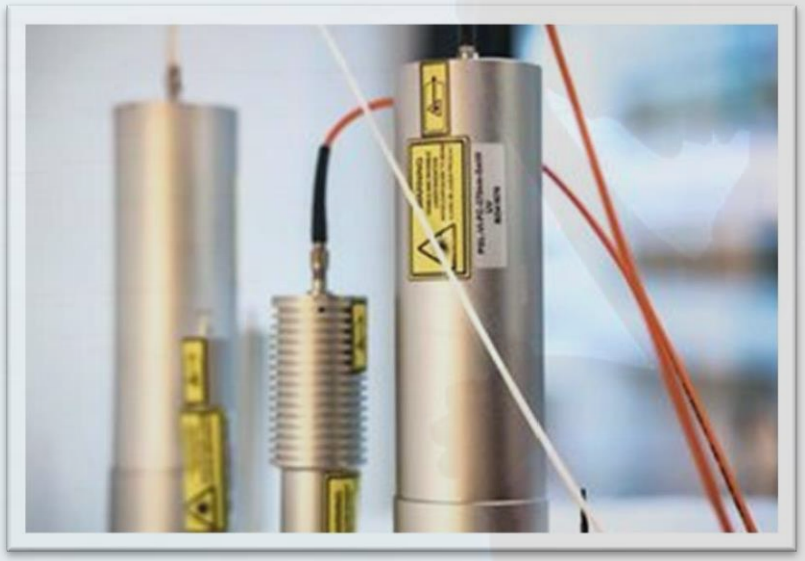
2020

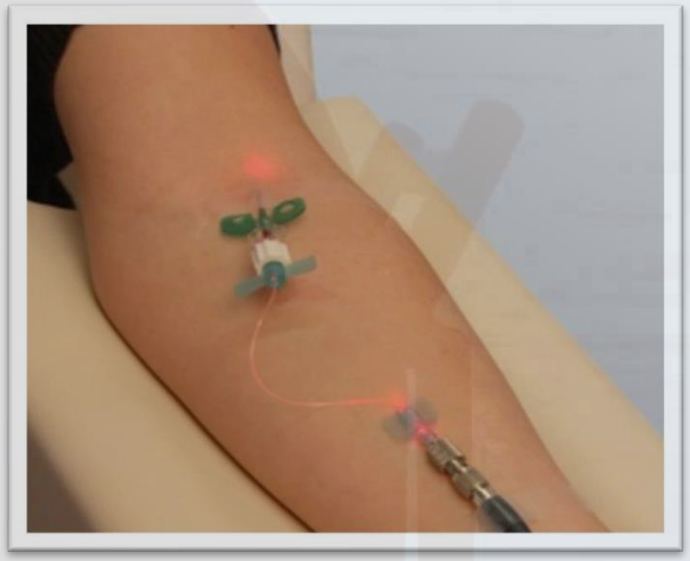
Clinical Trial > Lasers Med Sci. 2020 Dec;35(9):1945-1954. doi: 10.1007/s10103-020-02983-7.
Epub 2020 Mar 7.

Study of transcranial photobiomodulation at 945-nm wavelength: anxiety and depression

Transcranial photobiomodulation is an innovative method for the stimulation of neural activity which consists of the exposure of neural tissue to low-level light irradiance. In the present study, light-emitting diodes (LEDs) were used as light source due to their practicality and low cost. The objective was to analyze the effects of transcranial photobiomodulation using 945-nm LED in university students with anxiety and depression. Sample was composed of 22 individuals (17-25 years of age) divided into 2 groups of 11. LED group was treated with 945-nm LEDs for 1 min and 25 s (9.35 J/cm^2), while in the placebo group, the device was off when placed in contact with the frontal bone for the same amount of time as in treatment group. Participants were evaluated at baseline and after 30 days with the hospital anxiety and depression scale (HADS), the faces test, the designs test, and the grip strength test. On the HADS for anxiety, the mean PAB, PAA, PhAB, and PhAA were 13.89 ± 3.55, 12.82 ± 3.18, 10.75 ± 2.49, and 6.66 ± 2.50 points, respectively. In the HADS for depression, the mean for the PDB group was 13.89 ± 3.55 points, in the PhDB group 12.82 ± 3.18 points, in the PDA group 10.75 ± 2.49 points, and in the PhDA group 6.66 ± 2.50 points. In the PA and PD groups, mean values of 8.0 ± 1.5 and 8.9 ± 1.26 scores were obtained, but did not reach significance; however, between PA and PhD analysis, a significance level of p = 0.0003 was obtained. The 945-nm LED transcranial photobiomodulation improves brain activity and may clinically decrease anxiety and depression.

Excursos: IV- LLLT for Depression





Among many other beneficial effects, the Weberneedle® Endolaser with intravenous red, green, blue, yellow and ultraviolet light can help reduce systemic inflammations, and support mitochondrial function as well as the immune system and thus gut health.

Psychological and Mental Disorders: Anxiety

Human studies: T-LLLT for Anxiety

2019

Clinical Trial > Photobiomodul Photomed Laser Surg. 2019 Oct;37(10):644-650.
doi: 10.1089/photob.2019.4677.

Transcranial Photobiomodulation with Near-Infrared Light for Generalized Anxiety Disorder: A Pilot Study

Objective: Our aim was to test the anxiolytic effect of transcranial photobiomodulation (t-PBM) with near-infrared light (NIR) in subjects suffering from generalized anxiety disorder (GAD). ***Background:*** t-PBM with NIR is an experimental, noninvasive treatment for mood and anxiety disorders. Preliminary evidence indicates a potential anxiolytic effect of transcranial NIR. ***Methods:*** Fifteen subjects suffering from GAD were recruited in an open-label 8-week study. Each participant self-administered t-PBM daily, for 20 min (continuous wave; 830 nm peak wavelength; average irradiance 30 mW/cm^2; average fluence 36 J/cm^2; total energy delivered per session 2.9 kJ: total output power 2.4 W) broadly on the forehead (total area 80 cm^2) with an LED-cluster headband (Cerebral Sciences). Outcome measures were the reduction in total scores of the Hamilton Anxiety Scale (SIGH-A), the Clinical Global Impressions-Severity (CGI-S) subscale and the Pittsburgh Sleep Quality Index (PSQI) subscales from baseline to last observation carried forward. ***Results:*** Of the 15 recruited subjects (mean age 30 ± 14 years; 67% women), 12 (80%) completed the open trial. Results show a significant reduction in the total scores of SIGH-A (from 17.27 ± 4.89 to 8.47 ± 4.87; $p < 0.001$; Cohen's d effect size = 1.47), in the CGI-S subscale (from 4.53 ± 0.52 to 2.87 ± 0.83; $p < 0.001$; Cohen's d effect size = 2.04), as well as significant improvements in sleep at the PSQI. t-PBM was well tolerated with no serious adverse events. ***Conclusions:*** Based on our pilot study, t-PBM with NIR is a promising alternative treatment for GAD. Larger, randomized, double-blind, sham-controlled studies are needed.

Human studies: T-LLLT for Anxiety

2020

Clinical Trial > Lasers Med Sci. 2020 Dec;35(9):1945-1954. doi: 10.1007/s10103-020-02983-7.
Epub 2020 Mar 7.

Study of transcranial photobiomodulation at 945-nm wavelength: anxiety and depression

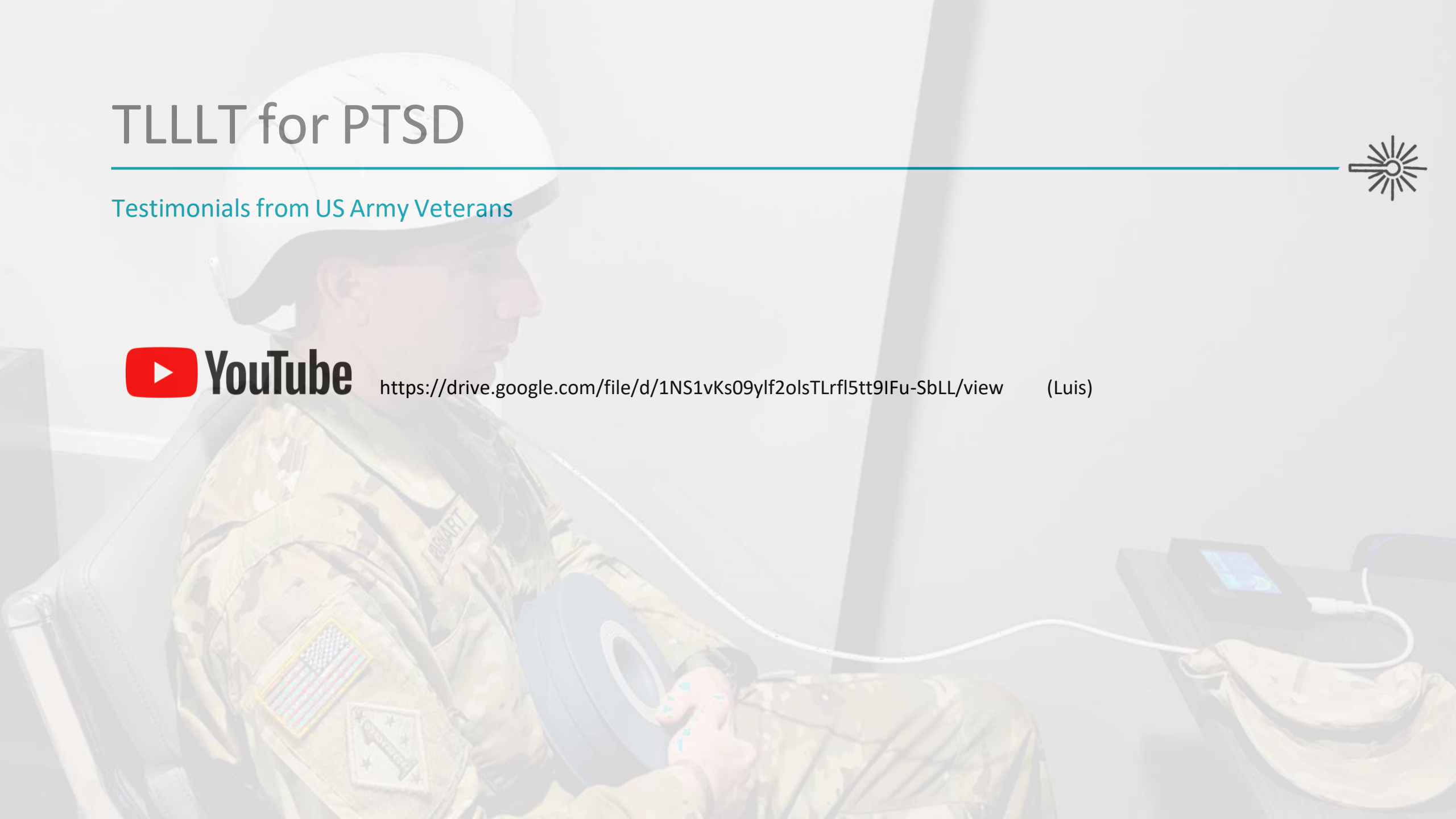
Transcranial photobiomodulation is an innovative method for the stimulation of neural activity which consists of the exposure of neural tissue to low-level light irradiance. In the present study, light-emitting diodes (LEDs) were used as light source due to their practicality and low cost. The objective was to analyze the effects of transcranial photobiomodulation using 945-nm LED in university students with anxiety and depression. Sample was composed of 22 individuals (17-25 years of age) divided into 2 groups of 11. LED group was treated with 945-nm LEDs for 1 min and 25 s (9.35 J/cm^2), while in the placebo group, the device was off when placed in contact with the frontal bone for the same amount of time as in treatment group. Participants were evaluated at baseline and after 30 days with the hospital anxiety and depression scale (HADS), the faces test, the designs test, and the grip strength test. On the HADS for anxiety, the mean PAB, PAA, PhAB, and PhAA were 13.89 ± 3.55, 12.82 ± 3.18, 10.75 ± 2.49, and 6.66 ± 2.50 points, respectively. In the HADS for depression, the mean for the PDB group was 13.89 ± 3.55 points, in the PhDB group 12.82 ± 3.18 points, in the PDA group 10.75 ± 2.49 points, and in the PhDA group 6.66 ± 2.50 points. In the PA and PD groups, mean values of 8.0 ± 1.5 and 8.9 ± 1.26 scores were obtained, but did not reach significance; however, between PA and PhD analysis, a significance level of p = 0.0003 was obtained. The 945-nm LED transcranial photobiomodulation improves brain activity and may clinically decrease anxiety and depression.

PTSD

Psychological and Mental Disorders

TLLLT for PTSD

Testimonials from US Army Veterans



YouTube https://drive.google.com/file/d/1NS1vKs09ylf2olsTLrfl5tt9IFu-SbLL/view (Luis)

Autism Spectrum Disorder

Neurodevelopmental Indications

The rationale for T-LLLT in the treatment of Autism Spectrum Disorder

Genetic and epigenetic causes (infections, toxins, poor nutrition, and inflammation during early pregnancy) can lead to issues at the mechanistic level:

- **increasing evidence that mitochondrial dysfunction is associated with autism**: Measurement of biomarkers associated with mitochondrial dysfunction and electron transport chain activity has suggested that up to 80% of children with ASD could have abnormal mitochondrial functions. Moreover, in the brain, there is evidence that disturbances in synaptic development, neuroplasticity, and signaling are associated with ASD.

Frye RE. Mitochondrial dysfunction in autism spectrum disorder: unique abnormalities and targeted treatments. Semin Pediatr Neurol 2020;35:100829.

Ebrahimi-Fakhari D, Sahin M. Autism and the synapse: emerging mechanisms and mechanism-based therapies. Curr Opin Neurol 2015;28:91–102.

- There is also evidence that **impairments in neurogenesis** (the forma-tion of new cortical neurons from progenitor cells in thebrain) is **involved in ASD**.

Bicker F, Nardi L, Maier J, Vasic V, Schmeisser MJ. Criss-crossing autism spectrum disorder and adult neurogenesis. J Neurochem 2021;159:452–478.

- Another type of pathology that has been **associated with ASD is excessive neuroinflammation**, possibly due to histaminergic neurotransmission.

Eissa N, Sadeq A, Sasse A, Sadek B. Role of neuroinflammation in autism spectrum disorder and the emergence of brain histaminergic system. Lessons also for BPSD? Front Pharmacol 2020;11

ASD studies on children and adolescents

2018

Clinical Trial > Adv Exp Med Biol. 2018;1116:111-130. doi: 10.1007/5584_2018_234.

Effects of Low-Level Laser Therapy in Autism Spectrum Disorder

Gerry Leisman [1 2 3], Calixto Machado [4], Yanin Machado [4], Mauricio Chinchilla-Acosta [4]

Abstract

The study examined the efficacy of low-level laser therapy, a form of photobiomodulation, for the treatment of irritability associated with autistic spectrum disorder in children and adolescents aged 5-17 years. Twenty-one of the 40 participants received eight 5-min procedures administered to the base of the skull and temporal areas across a 4-week period (test, i.e., active treatment participants). All the participants were evaluated with the Aberrant Behavior Checklist (ABC), with the global scale and five subscales (irritability/agitation, lethargy/social withdrawal, stereotypic behavior, hyperactivity/noncompliance, and inappropriate speech), and the Clinical Global Impressions (CGI) Scale including a severity-of-illness scale (CGI-S) and a global improvement/change scale (CGI-C). The evaluation took place at baseline, week 2 (interim), week 4 (endpoint), and week 8 (post-procedure) of the study. The adjusted mean difference in the baseline to study endpoint change in the ABC irritability subscale score between test and placebo participants was -15.17 in favor of the test procedure group. ANCOVA analysis found this difference to be statistically significant ($F = 99.34$, $p < 0.0001$) compared to the baseline ABC irritability subscale score. The study found that low-level laser therapy could be an effective tool for reducing irritability and other symptoms and behaviors associated with the autistic spectrum disorder in children and adolescents, with positive changes maintained and augmented over time.

ASD studies on children and adolescents

2022

Children (Basel). 2022 May 20;9(5):755. doi: 10.3390/children9050755.

Transcranial Photobiomodulation for the Treatment of Children with Autism Spectrum Disorder (ASD): A Retrospective Study

Stefano Pallanti [1] [2], Michele Di Ponzio [1], Eleonora Grassi [1], Gloria Vannini [1], Gilla Cauli [3]

Abstract

Children with Autism Spectrum Disorder (ASD) face several challenges due to deficits in social function and communication along with restricted patterns of behaviors. Often, they also have difficult-to-manage and disruptive behaviors. At the moment, there are no pharmacological treatments for ASD core features. Recently, there has been a growing interest in non-pharmacological interventions for ASD, such as neuromodulation. In this retrospective study, data are reported and analyzed from 21 patients (13 males, 8 females) with ASD, with an average age of 9.1 (range 5-15), who received six months of transcranial photobiomodulation (tPBM) at home using two protocols (alpha and gamma), which, respectively, modulates the alpha and gamma bands. They were evaluated at baseline, after three and six months of treatment using the Childhood Autism Rating Scale (CARS), the Home Situation Questionnaire-ASD (HSQ-ASD), the Autism Parenting Stress Index (APSI), the Montefiore Einstein Rigidity Scale-Revised (MERS-R), the Pittsburgh Sleep Quality Index (PSQI) and the SDAG, to evaluate attention. Findings show that tPBM was associated with a reduction in ASD severity, as shown by a decrease in CARS scores during the intervention (p < 0.001). A relevant reduction in noncompliant behavior and in parental stress have been found. Moreover, a reduction in behavioral and cognitive rigidity was reported as well as an improvement in attentional functions and in sleep quality. Limitations were discussed as well as future directions for research.

ASD studies on adults

2022

Photobiomodul Photomed Laser Surg. 2022 Jan;40(1):4-12. doi: 10.1089/photob.2020.4986. Epub 2021 Dec 23.

Transcranial Photobiomodulation in Adults with High-Functioning Autism Spectrum Disorder: Positive Findings from a Proof-of-Concept Study

Objective: To assess the efficacy and safety of transcranial photobiomodulation (tPBM) in adults with autism spectrum disorder (ASD). ***Methods:*** Adults with high-functioning-ASD, between 18 and 59 years of age, were enrolled to receive twice a week tPBM for 8 weeks in an open-label single group design. ASD symptom severity was assessed at baseline, midpoint, and end-point, by clinician-, self-, and informant-rated measures. Treatment response was defined as a ≥30% reduction in Social Responsiveness Scale-2nd Edition (SRS-2) total score and ASD Clinical Global Impression-Improvement score ≤2. Any possible adverse events were recorded at each visit. Paired-samples *t*-test analyses were performed. ***Results:*** Eleven participants were enrolled, and 10 participants (9 males; 30.0 ± 11.9 years) completed the study. One participant withdrew consent before baseline. All 10 completers were included in efficacy and safety analyses. Five participants (50%) met responder criteria at end-point. Overall, 8-week tPBM was associated with significant reduction in SRS-2 total scores at end-point (SRS-2: -30.6 ± 23, $p < 0.001$) particularly in Social Awareness (-3.0 ± 1.9, $p < 0.001$), Social Communication (-10.3 ± 6, $p < 0.001$), Social Motivation (-5.0 ± 2.4, $p < 0.001$), and Restricted/Repetitive Behaviors (-7.4 ± 4.1, $p < 0.001$). There were statistically significant improvements at end-point in Global Assessment of Functioning scores (+12.8 ± 4.2, $p < 0.001$) and Quality of Life Enjoyment and Satisfaction Questionnaire scores (+6.0 ± 7.9, $p = 0.02$). Three participants experienced transient, mild side effects (insomnia, headache, and warmth at treatment application site). No adverse events required changes in tPBM protocol. Adherence rate was 98%. ***Conclusions:*** tPBM is a safe and feasible treatment approach that has the potential to treat core features of ASD. Further research is necessary and warranted. ClinicalTrials.gov Identifier:

Traumatic Brain Injuries

Human studies: TBI

2014

JOURNAL OF NEUROTRAUMA
Mary Ann Liebert, Inc. publishers
Journals | Search | Alerts

J Neurotrauma. 2014 Jun 1; 31(11): 1008–1017.
doi: 10.1089/neu.2013.3244

PMCID: PMC4043367
PMID: 24568233

Significant Improvements in Cognitive Performance Post-Transcranial, Red/Near-Infrared Light-Emitting Diode Treatments in Chronic, Mild Traumatic Brain Injury: Open-Protocol Study

Margaret A. Naeser,[1,2] Ross Zafonte,[3,4] Maxine H. Krengel,[1,2] Paula I. Martin,[1,2] Judith Frazier,[3] Michael R. Hamblin,[5] Jeffrey A. Knight,[6] William P. Meehan, III,[7] and Errol H. Baker[1]

Administration [FDA], an insignificant risk device). Eleven chronic, mTBI participants (26–62 years of age, 6 males) with nonpenetrating brain injury and persistent cognitive dysfunction were treated for 18 outpatient sessions (Monday, Wednesday, Friday, for 6 weeks), starting at 10 months to 8 years post- mTBI (motor vehicle accident [MVA] or sports-related; and one participant, improvised explosive device [IED] blast injury). Four had a history of multiple concussions. Each LED cluster head (5.35 cm diameter, 500 mW, 22.2 mW/cm^2) was applied for 10 min to each of 11 scalp placements (13 J/cm^2). LEDs were placed on the midline from front-to-back hairline; and bilaterally on frontal, parietal, and temporal areas. Neuropsychological testing was performed pre-LED, and at 1 week, and 1 and 2 months after the 18th treatment. A significant linear trend was observed for the effect of LED treatment over time for the Stroop test for Executive Function, Trial 3 inhibition (p=0.004); Stroop, Trial 4 inhibition switching (p=0.003); California Verbal Learning Test (CVLT)-II, Total Trials 1–5 (p=0.003); and CVLT-II, Long Delay Free Recall (p=0.006). Participants reported improved sleep, and fewer post-traumatic stress disorder (PTSD) symptoms, if present. Participants and family reported better ability to perform social, interpersonal, and occupational functions. These open-protocol data suggest that placebo-controlled studies are warranted.

Human studies: TBI

2018

› Photomed Laser Surg. 2018 Nov 28. doi: 10.1089/pho.2018.4489. Online ahead of print.

Pulsed Transcranial Red/Near-Infrared Light Therapy Using Light-Emitting Diodes Improves Cerebral Blood Flow and Cognitive Function in Veterans with Chronic Traumatic Brain Injury: A Case Series

Materials and methods: Twelve symptomatic military Veterans diagnosed with chronic TBI >18 months post-trauma received pulsed transcranial PBMT (tPBMT) using two neoprene therapy pads containing 220 infrared and 180 red LEDs, generating a power output of 3.3 W and an average power density of 6.4 mW/cm^2 for 20 min, thrice per week over 6 weeks. Outcome measures included standardized neuropsychological test scores and qualitative and quantitative single photon emission computed tomography (SPECT) measures of regional cerebral blood flow (rCBF).

Results: Pulsed tPBMT significantly improved neuropsychological scores in 6 of 15 subscales (40.0%; $p < 0.05$; two tailed). SPECT analysis showed increase in rCBF in 8 of 12 (66.7%) study participants. Quantitative SPECT analysis revealed a significant increase in rCBF in this subgroup of study participants and a significant difference between pre-treatment and post-treatment gamma ray counts per cubic centimeter [$t = 3.77$, $df = 7$, $p = 0.007$, 95% confidence interval (95,543.21-21,931.82)]. This is the first study to report quantitative SPECT analysis of rCBF in regions of interest following pulsed tPBMT with LEDs in TBI.

Conclusions: Pulsed tPBMT using LEDs shows promise in improving cognitive function and rCBF several years after TBI. Larger, controlled studies are indicated.

Researchers tested
73 Hz, 587 Hz, and 1175 Hz

Human studies: TBI

2020

JAMA Netw Open. 2020 Sep; 3(9): e2017337.
Published online 2020 Sep 14. doi: 10.1001/jamanetworkopen.2020.17337
PMCID: PMC7490644
PMID: 32926117

Effect of Transcranial Low-Level Light Therapy vs Sham Therapy Among Patients With Moderate Traumatic Brain Injury

Results

Of the 68 patients who were randomized (33 to LLLT and 35 to sham therapy), 28 completed at least 1 LLLT session. No adverse events referable to LLLT were reported. Forty-three patients (22 men [51.2%]; mean [SD] age, 50.49 [17.44] years]) completed the study with at least 1 magnetic resonance imaging scan: 19 individuals in the LLLT group and 24 in the sham treatment group. Radial diffusivity (RD), mean diffusivity (MD), and fractional anisotropy (FA) showed significant time and treatment interaction at 3-month time point (RD: 0.013; 95% CI, 0.006 to 0.019; $P < .001$; MD: 0.008; 95% CI, 0.001 to 0.015; $P = .03$; FA: −0.018; 95% CI, −0.026 to −0.010; $P < .001$).The LLLT group had lower RPQ scores, but this effect did not reach statistical significance (time effect $P = .39$, treatment effect $P = .61$, and time × treatment effect $P = .91$).

Conclusions and Relevance

In this randomized clinical trial, LLLT was feasible in all patients and did not exhibit any adverse events. Light therapy altered multiple diffusion tensor parameters in a statistically significant manner in the late subacute stage. This study provides the first human evidence to date that light therapy engages neural substrates that play a role in the pathophysiologic factors of moderate TBI and also suggests diffusion imaging as the biomarker of therapeutic response.

Low-level light therapy at 810nm was provided by a custom-built helmet outfitted with 18 clusters of 20 NIR light-emitting diodes. It was started within 72 hours after the TBI. Treatment was divided into 3 sessions of 20 minutes' duration with at least 12-hour intervals between the therapy sessions. The helmet provided an incident fluence of approximately 43 J/cm^2 (0.036 W/cm^2 × 20 minutes ×60 seconds/min = 43.2 J/cm^2) to the scalp per 20-minute session.
Based on known scalp/skull transmission of NIR light in cadavers, approximately 3% (or 1.3 J/cm^2) of the incident fluence reached the cortical surface of the brain.

Stroke

Human studies: Stroke

2007

Randomized Controlled Trial > Stroke. 2007 Jun;38(6):1843-9.
doi: 10.1161/STROKEAHA.106.478230. Epub 2007 Apr 26.

Infrared laser therapy for ischemic stroke: a new treatment strategy: results of the NeuroThera Effectiveness and Safety Trial-1 (NEST-1)

Results: Mean time to treatment was >16 hours (median time to treatment 18 hours for active and 17 hours for control). Time to treatment ranged from 2 to 24 hours. More patients (70%) in the active treatment group had successful outcomes than did controls (51%), as measured prospectively on the bNIH (P=0.035 stratified by severity and time to treatment; P=0.048 stratified only by severity). Similarly, more patients (59%) had successful outcomes than did controls (44%) as measured at 90 days as a binary mRS score of 0 to 2 (P=0.034 stratified by severity and time to treatment; P=0.043 stratified only by severity). Also, more patients in the active treatment group had successful outcomes than controls as measured by the change in mean NIHSS score from baseline to 90 days (P=0.021 stratified by time to treatment) and the full mRS ("shift in Rankin") score (P=0.020 stratified by severity and time to treatment; P=0.026 stratified only by severity). The prevalence odds ratio for bNIH was 1.40 (95% CI, 1.01 to 1.93) and for binary mRS was 1.38 (95% CI, 1.03 to 1.83), controlling for baseline severity. Similar results held for the Barthel Index and Glasgow Outcome Scale. Mortality rates and serious adverse events (SAEs) did not differ significantly (8.9% and 25.3% for active 9.8% and 36.6% for control, respectively, for mortality and SAEs).

Conclusions: The NEST-1 study indicates that infrared laser therapy has shown initial safety and effectiveness for the treatment of ischemic stroke in humans when initiated within 24 hours of stroke onset. A larger confirmatory trial to demonstrate safety and effectiveness is warranted.

Human studies: Stroke

2009

Randomized Controlled Trial > Stroke. 2009 Apr;40(4):1359-64.
doi: 10.1161/STROKEAHA.109.547547. Epub 2009 Feb 20.

Effectiveness and safety of transcranial laser therapy for acute ischemic stroke

= „NEST II“

Results: We randomized 660 patients: 331 received TLT and 327 received sham; 120 (36.3%) in the TLT group achieved favorable outcome versus 101 (30.9%), in the sham group (P=0.094), odds ratio 1.38 (95% CI, 0.95 to 2.00). Comparable results were seen for the other outcome measures. Although no prespecified test achieved significance, a post hoc analysis of patients with a baseline National Institutes of Health Stroke Scale score of <16 showed a favorable outcome at 90 days on the primary end point (P<0.044). Mortality rates and serious adverse events did not differ between groups with 17.5% and 17.4% mortality, 37.8% and 41.8% serious adverse events for TLT and sham, respectively.

Conclusions: TLT within 24 hours from stroke onset demonstrated safety but did not meet formal statistical significance for efficacy. However, all predefined analyses showed a favorable trend, consistent with the previous clinical trial (NEST-1). Both studies indicate that mortality and adverse event rates were not adversely affected by TLT. A definitive trial with refined baseline National Institutes of Health Stroke Scale exclusion criteria is planned.

Human studies: Stroke

2014

Clinical Trial > Stroke. 2014 Nov;45(11):3187-93. doi: 10.1161/STROKEAHA.114.005795.
Epub 2014 Oct 7.

Transcranial laser therapy in acute stroke treatment: results of neurothera effectiveness and safety trial 3, a phase III clinical end point device trial

= „NEST III“

Results: The study was terminated on recommendation by the Data Monitoring Committee after a futility analysis of 566 completed patients found no difference in the primary end point (transcranial laser therapy 140/282 [49.6%] versus sham 140/284 [49.3%] for good functional outcome; modified Rankin Scale, 0-2). The results remained stable after inclusion of all 630 randomized patients (adjusted odds ratio, 1.024; 95% confidence interval, 0.705-1.488).

Conclusions: Once the results of the interim futility analysis became available, all study support was immediately withdrawn by the capital firms behind PhotoThera, and the company was dissolved. Proper termination of the trial was difficult but was finally achieved through special efforts by former employees of PhotoThera, the CRO Parexel and members of the steering and the safety committees. We conclude that transcranial laser therapy does not have a measurable neuroprotective effect in patients with acute ischemic stroke when applied within 24 hours after stroke onset.

Human studies: Stroke

2022

doi: 10.1089/photob.2022.0042. Epub 2022 Oct 10.

Intravascular Laser Irradiation of Blood Improves Functional Independence in Subacute Post-Stroke Patients: A Retrospective Observational Study from a Post-Stroke Acute Care Center in Taiwan

= IV- PBM !

Objective: To investigate the effect of intravascular laser irradiation of blood (ILIB) in patients with post-stroke disability. ***Background:*** Helium-neon intravascular laser at a wavelength of 632.8 nm has been applied in post-stroke rehabilitation for many years in Taiwan. Data were collected from our practice to validate its effectiveness. ***Materials and methods:*** This was a single-center, retrospective, observational study. Data from 34 patients with first-episode ischemic stroke who participated in the post-acute care program and had an initial modified Rankin Scale (mRS) score of 4 between July 2018 and June 2021 were retrospectively reviewed. Twelve patients who received conventional rehabilitation plus ILIB were in the ILIB group. Twenty-two patients who received conventional rehabilitation only were in the control group. Assessments, including the mRS, Barthel Index (BI), Berg Balance Scale (BBS), 6-min walk test (6MWT), and Fugl-Meyer Assessment of the upper extremity (FMA-UE), were performed to evaluate any post-treatment improvement. ***Results:*** Patients who received ILIB had significantly superior mRS scores than those who received only conventional rehabilitation (p = 0.028). Patients in the ILIB group experienced more improvements in the BI, 6MWT, and FMA-UE; however, these were nonsignificant. In addition, the control group experienced a greater improvement in the BBS than the ILIB group. Further studies are required to elucidate the mechanism of action of ILIB therapy fully. There was no major adverse event reported in patients receiving ILIB therapy. ***Conclusions:*** ILIB improved independence in post-stroke patients, suggesting that ILIB is a promising treatment for facilitating post-stroke recovery.

Migraine

Other Neurological Disorders

Review: tPBM for headache

2020

Review > Life (Basel). 2022 Jan 11;12(1):98. doi: 10.3390/life12010098.

Photobiomodulation for the Treatment of Primary Headache: Systematic Review of Randomized Clinical Trials

Abstract

The purpose of this study was to evaluate the efficacy and safety of photobiomodulation as an adjuvant treatment for primary headache. A systematic review of randomized clinical trials was performed. For such, electronic searches were performed in the MEDLINE, Embase, Cochrane Library, LILACS, PEDro, PsycInfo, Clinicaltrials.gov., and WHO/ICTRP databases, with no restrictions imposed regarding language or year of publication. We included studies that assessed any photobiomodulation therapy as an adjuvant treatment for primary headache compared to sham treatment, no treatment, or another intervention. The methodological assessment was conducted using the Cochrane Risk of Bias tool. The certainty of the evidence was classified using the GRADE approach. Four randomized clinical trials were included. Most of the included studies had an overall high risk of bias. Compared to sham treatment, photobiomodulation had a clinically important effect on pain in individuals with primary headache. Despite the benefits reported for other outcomes, the estimates were imprecise, and the certainty of the evidence was graded as low. These findings are considered insufficient to support the use of photobiomodulation in the treatment of primary headache. Randomized clinical trials, with higher methodological quality, are needed to enhance the reliability of the estimated effects.

Keywords: low-level laser; pain; photobiomodulation; primary headache.

Improvement of cognitive function in healthy individuals

Human studies: tPBM to improve cognitive functions

2013

Photobiomodulation, Photomedicine, and Laser Surgery
Volume 37, Number 10, 2019

Pp. 635–643
DOI: 10.1089/photob.2019.4673

Transcranial Photobiomodulation Improves Cognitive Performance in Young Healthy Adults: A Systematic Review and Meta-Analysis

Methods: We searched MEDLINE using PubMed, EMBASE, SCOPUS, Web of Science, and Cochrane Library up to March 2019. We also searched ProQuest and Google Scholar databases for unpublished material. The search was limited to articles on the procognitive effects of t-PBM in healthy adults. The initial search resulted in 871 studies, of which nine publications met our criteria for inclusion and exclusion. Seven studies were performed on young, healthy subjects (17–35 years), and two studies were conducted on older (≥49 years), normal subjects. A meta-analysis was performed on six full-text publications whose subjects were young adults.
Results: t-PBM administration improved cognition-related outcomes by an 0.833 standardized mean difference (SMD; 95% confidence interval (CI): 0.458–1.209, 14 comparisons) in young, healthy participants. Funnel plotting revealed asymmetry, which was validated using Egger's ($p=0.030$) and Begg's regression ($p=0.006$) tests. However after reanalysis, this asymmetry disappeared in the attention subgroup, but not in the memory subgroup. The trim-and-fill analysis indicated two studies were lacking required data. Thus, the effect size was adjusted from an SMD of 0.761 (95% CI: 0.573–0.949) to 0.949 (0.779–1.120). The overall quality score of the studies was modest.
Conclusions: We demonstrated a significant, beneficial effect of t-PBM on cognitive performance of young, healthy individuals; however, the heterogeneity of the data was high. This could be due to the modest quality or to the low number of included studies, or to the differences between the various subdomains assessed. These shortcomings should be meticulously addressed before concluding that t-PBM is a cognitive-enhancing intervention in healthy individuals.

Summary: Transcranial Photobiomodulation

- works on a fundamental level and helps the brain improve / restore its natural functions
- very promising data for different „brain disorders“
- also an interesting method for healthy individuals: (likely) improvement of cognitive functions & prevention
- current limitations:
  - →lack of understanding of the detailed mechanisms
  - →mostly small sample sizes in studies = larger studies needed
  - → not always highest quality of studies
- side-effect-free / safe therapy
- can be done at home

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LED Infrared Helmet

Weber Medical

Weber Medical GmbH

One of the world's leading companies in medical laser technology

- Established in 2003 after many years of research and development in the field of medical lasers
- Received financial aid from the German government and the European Union in 2004 for the development of the world's first multichannel laser systems for invasive laser therapy: CE approval for different laser machines since 2005

Main location in Lauenförde, Germany

- Focus on evidence-based medicine: Cooperation with several research institutions
- 12 years of clinical experience with data from more than 1,500 clinics worldwide
- Weber Medical operates treatment and training centers in Germany and Thailand
- With the aim of building a worldwide distribution, research and education network the company founded the International Society for Medical Laser Applications (ISLA e.V.) in 2006
- Weber Medical is undertaking constant research and development in cooperation with different universities worldwide to ensure high standards and a continuous development of the products

Scientific Partnerships

International Research Networks

GEORG-AUGUST-UNIVERSITÄT GÖTTINGEN

ISLA RESEARCH GROUP
International Society for Medical Laser Applications

Philipps Universität Marburg

NAALT
North American Association for PhotobiomoduLation Therapy

ISLA
International Society for Medical Laser Applications

Medizinische Universität Graz

UNIVERSITAS STUDIORUM MUTINENSIS ET REG.

UNIM

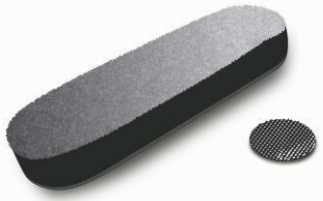
Learning For Community Service
ONDO STATE UNIVERSITY OF MEDICAL SCIENCES

MAYO CLINIC

1972
FACULTY OF MEDICINE
KHON KAEN UNIVERSITY

LED Infrared Helmet

Recharge Your Brain!



Comes with foam pads in order to adjust size and increase wearing comfort

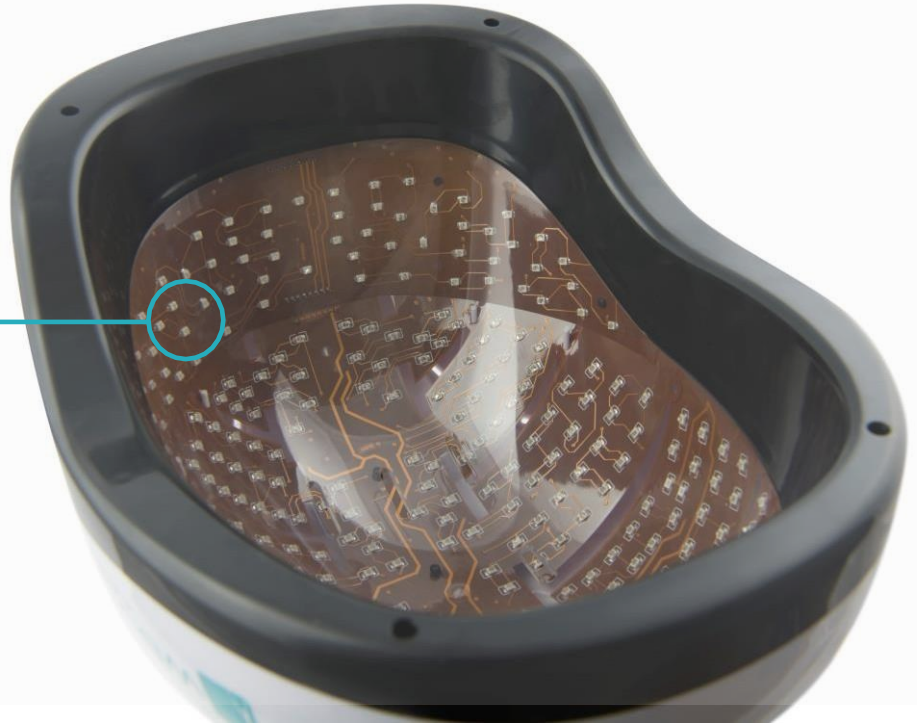
Technical Details

Number of diodes: 320

Wavelength: 810 nm

Power: 50 mW/diode

Total power: 16 W



LED Infrared Helmet

Easy Handling

Treatment time: 1-30 minutes

Recommendation: 15-30 minutes (1-2x per day)

4 Intensity levels (25-50-75-100%)

Frequency from 1 Hz to 20,000 Hz

Resources

Substack (Newsletter & Blog) about Photobiomodulation Therapy and Mental Health by Martin Junggebauer
https://lightandequanimity.substack.com

Webinar by Michael Ellenburg, ND, MPH, LAc (USA)
https://www.youtube.com/watch?v=mNB7s3uusZg&t=3520s

Photobiomodulation-Therapy Research Database (6.000+ studies)
(Click here)

Protocol Book: Application of the Weber Medical LED Infrared Helmet
(request by email)

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+4917620297881

Literature

Alzheimer´s and Dementia

a) Human studies

(2017) 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):432-441. doi:10.1089/pho.2016.4227

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https://alz-journals.onlinelibrary.wiley.com/doi/epdf/10.1002/alz.054945

b) Animal studies

(2021) Salehpour F, Khademi M, Hamblin MR. Photobiomodulation Therapy for Dementia: A Systematic Review of Pre-Clinical and Clinical Studies. J Alzheimers Dis. 2021;83(4):1431-1452. doi: 10.3233/JAD-210029. PMID: 33935090.

Literature

Parkinson´s

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