

Photobiomodulation (PBM) / Low Level laser Therapy (LLLT)

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Notes: A selection of recent papers demonstrating cognition - and mood enhancing effects of PBMT

Beneficial neurocognitive effects of transcranial laser in older adults.

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Transcranial infrared laser stimulation (TILS) at 1064 nm, 250 mW/cm² has been proven safe and effective for increasing neurocognitive functions in young adults in controlled studies using photobiomodulation of the right prefrontal cortex. The objective of this pilot study was to determine whether there is any effect from TILS on neurocognitive function in older adults with subjective memory complaint at risk for cognitive decline (e.g., increased carotid artery intima-media thickness or mild traumatic brain injury). We investigated the cognitive effects of TILS in older adults (ages 49-90, n = 12) using prefrontal cortex measures of attention (psychomotor vigilance task (PVT)) and memory (delayed match to sample (DMS)), carotid artery intima-media thickness (measured by ultrasound), and evaluated the potential neural mechanisms mediating the cognitive effects of TILS using exploratory brain studies of electroencephalography (EEG, n = 6) and functional magnetic resonance imaging (fMRI, n = 6). Cognitive performance, age, and carotid artery intima-media thickness were highly correlated, but all participants improved in all cognitive measures after TILS treatments. Baseline vs. chronic (five weekly sessions, 8 min each) comparisons of mean cognitive scores all showed improvements, significant for PVT reaction time (p < 0.001), PVT lapses (p < 0.001), and DMS correct responses (p < 0.05). The neural studies also showed for the first time that **TILS increases resting-state EEG alpha, beta, and gamma power and promotes more efficient prefrontal blood-oxygen-level-dependent (BOLD)-fMRI response**. Importantly, no adverse effects were found. These preliminary findings support the use of TILS for larger randomized clinical trials with this non-invasive approach to **augment neurocognitive function in older people to combat aging-related and vascular disease-related cognitive decline**.

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Transcranial, Red/Near-Infrared Light-Emitting Diode Therapy to Improve Cognition in Chronic Traumatic Brain Injury.

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OBJECTIVE: We review the general topic of traumatic brain injury (TBI) and our research utilizing transcranial photobiomodulation (tPBM) to improve cognition in chronic TBI using red/near-infrared (NIR) light-emitting diodes (LEDs) to deliver light to the head. tPBM improves mitochondrial function increasing oxygen consumption, production of adenosine triphosphate (ATP), and improving cellular energy stores. Nitric oxide is released from the cells increasing regional blood flow in the brain. Review of published studies: In our previously published study, 11 chronic TBI patients with closed-head TBI caused by different accidents (motor vehicle accident, sports-related, improvised explosive device blast injury) and exhibiting long-lasting cognitive dysfunction received 18 outpatient treatments (Monday, Wednesday, Friday for 6 weeks) starting at 10 months to 8 years post-TBI. LED therapy is nonthermal, painless, and noninvasive. An LED-based device classified as nonsignificant risk (FDA cleared) was used. Each LED cluster head (5.35cm diameter, 500mW, 22.2mW/cm²) was applied for 9min 45sec (13J/cm²) using 11 locations on the scalp: midline from front-to-back hairline and bilaterally on frontal, parietal, and temporal areas. Testing was performed before and after transcranial LED (tLED; at 1 week, 1 month, and at 2 months after the 18th treatment) and showed **significant improvements in executive function and verbal memory**. There were also **fewer post-traumatic stress disorder (PTSD) symptoms** reported. Ongoing studies: Ongoing, current studies involve TBI patients who have been treated with tLED using either 26J/cm² per LED location on the head or treated with intranasal only (iLED) using red (633nm) and NIR (810nm) diodes placed into the nostrils. The NIR iLED is hypothesized to deliver photons to the hippocampus, and the red 633nm iLED is believed to increase melatonin. Results have been similar to the previously published tLED study. Actigraphy sleep data showed **increased time asleep** (on average one additional hour per night) after the 18th tLED or iLED treatment. LED treatments may be performed in the home. Sham-controlled studies with veterans who have cognitive dysfunction from Gulf War Illness, blast TBI, and TBI/PTSD are currently ongoing.

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Transcranial Laser Stimulation as Neuroenhancement for Attention Bias Modification in Adults with Elevated Depression Symptoms.

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BACKGROUND: Low-level light therapy (LLLT) with transcranial laser is a non-invasive form of neuroenhancement shown to regulate neuronal metabolism and cognition. Attention bias modification (ABM) is a cognitive intervention designed to improve depression by decreasing negative attentional bias, but to date its efficacy has been inconclusive. Adjunctive neuroenhancement to augment clinical effectiveness has shown promise, particularly for individuals who respond positively to the primary intervention. **OBJECTIVE/HYPOTHESIS:** This randomized, sham-controlled proof-of-principle study is the first to test the hypothesis that augmentative LLLT will improve the effects of ABM among adults with elevated symptoms of depression. **METHODS:** Fifty-one adult participants with elevated symptoms of depression received ABM before and after laser stimulation and were randomized to one of three conditions: right forehead, left forehead, or sham. Participants repeated LLLT two days later and were assessed for depression symptoms one and two weeks later. **RESULTS:** A significant three-way interaction between LLLT condition, ABM response, and time indicated that right LLLT led to greater symptom improvement among participants whose attention was responsive to ABM (i.e., attention was directed away from negative stimuli). Minimal change in depression was observed in the left and sham LLLT. **CONCLUSIONS:** The beneficial effects of ABM on depression symptoms may be enhanced when paired with adjunctive interventions such as right prefrontal LLLT; however, cognitive response to ABM likely moderates the impact of neuroenhancement. The results suggest that larger clinical trials examining the efficacy of using photoneuromodulation to augment cognitive training are warranted.

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Cognitive enhancement by transcranial laser stimulation and acute aerobic exercise.

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This is the first randomized, controlled study comparing the cognitive effects of transcranial laser stimulation and acute aerobic exercise on the same cognitive tasks. We examined whether transcranial infrared laser stimulation of the prefrontal cortex, acute high-intensity aerobic exercise, or the combination may enhance performance in sustained attention and working memory tasks. Sixty healthy young adults were randomly assigned to one of the following four treatments: (1) low-level laser therapy (LLLT) with infrared laser to two forehead sites while seated (total 8 min, 1064 nm continuous wave, 250 mW/cm², 60 J/cm² per site of 13.6 cm²); (2) acute exercise (EX) of high-intensity (total 20 min, with 10-min treadmill running at 85-90 % VO₂max); (3) combined treatment (LLLT + EX); or (4) sham control (CON). Participants were tested for prefrontal measures of sustained attention with the psychomotor vigilance task (PVT) and working memory with the delayed match-to-sample task (DMS) before and after the treatments. As compared to CON, both LLLT and EX reduced reaction time in the PVT [$F(1.56) = 4.134$, $p = 0.01$, $\eta^2 = 0.181$] and increased the number of correct responses in the DMS [$F(1.56) = 4.690$, $p = 0.005$, $\eta^2 = 0.201$], demonstrating a significant enhancing effect of LLLT and EX on cognitive performance. LLLT + EX effects were similar but showed no significantly greater improvement on PVT and DMS than LLLT or EX alone. The transcranial infrared laser stimulation and acute aerobic exercise treatments were similarly effective for cognitive enhancement, suggesting that they augment prefrontal cognitive functions similarly.

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Near-Infrared Transcranial Radiation for Major Depressive Disorder: Proof of Concept Study.

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Transcranial near-infrared radiation (NIR) is an innovative treatment for major depressive disorder (MDD), but clinical evidence for its efficacy is limited. Our objective was to investigate the tolerability and efficacy of NIR in patients with MDD. We conducted a proof of concept, prospective, double-blind, randomized study of 6 sessions of NIR versus sham treatment for patients with MDD, using a crossover design. Four patients with MDD with mean age 47 +/- 14 (SD) years (1 woman and 3 men) were exposed to irradiance of 700 mW/cm² and a fluence of 84 J/cm² for a total NIR energy of 2.40 kJ delivered per session for 6 sessions. Baseline mean **HAM-D17 scores decreased** from 19.8 +/- 4.4 (SD) to 13 +/- 5.35 (SD) after treatment ($t = 7.905$; $df = 3$; $P = 0.004$). Patients tolerated the treatment well without any serious adverse events. These **findings confirm and extend the preliminary data on NIR as a novel intervention for patients with MDD**, but further clinical trials are needed to better understand the efficacy of this new treatment. This trial is registered with ClinicalTrials.gov NCT01538199.

Psychiatry J 2015 2015 352979

<http://www.ncbi.nlm.nih.gov/pubmed/?term=26356811>

Transcranial infrared laser stimulation produces beneficial cognitive and emotional effects in humans.

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This is the first controlled study demonstrating the beneficial effects of transcranial laser stimulation on cognitive and emotional functions in humans. Photobiomodulation with red to near-infrared light is a novel intervention shown to regulate neuronal function in cell cultures, animal models, and clinical conditions. Light that intersects with the absorption spectrum of cytochrome oxidase was applied to the forehead of healthy volunteers using the laser diode CG-5000, which maximizes tissue penetration and has been used in humans for other indications. We tested whether low-level laser stimulation produces beneficial effects on frontal cortex measures of attention, memory and mood. Reaction time in a sustained-attention psychomotor vigilance task (PVT) was significantly improved in the treated (n=20) vs. placebo control (n=20) groups, especially in high novelty-seeking subjects. Performance in a delayed match-to-sample (DMS) memory task showed also a significant improvement in treated vs. control groups as measured by memory retrieval latency and number of correct trials. The Positive and Negative Affect Schedule (PANAS-X), which tracks self-reported positive and negative affective (emotional) states over time, was administered immediately before treatment and 2 weeks after treatment. The PANAS showed that while participants generally reported more positive affective states than negative, overall affect improved significantly in the treated group due to more sustained positive emotional states as compared to the placebo control group. These data imply that transcranial laser stimulation could be used as a non-invasive and efficacious approach to increase brain functions such as those related to cognitive and emotional dimensions. Transcranial infrared laser stimulation has also been proven to be safe and successful at improving neurological outcome in humans in controlled clinical trials of stroke. This innovative approach could lead to the development of non-invasive, performance-enhancing interventions in healthy humans and in those in need of neuropsychological rehabilitation.

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