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Infrared Laser Treatment of TBI, PTSD, and Depression: An Expert Perspective

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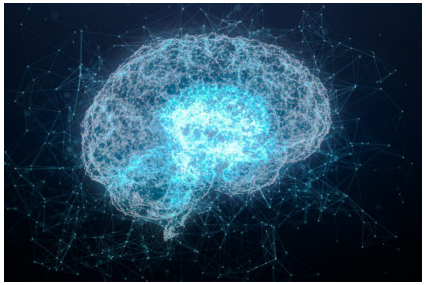
Disclosure: Dr Henderson is the president and principal owner of The Synaptic Space, a neuroimaging consulting firm, and owner of Neuro-Luminance Corporation. Please see the listed studies for a full list of disclosures.



When it comes to infrared light treatment, it is all a matter of getting there: the infrared light must be able to penetrate all the overlying tissue to reach the brain.

During the last 20 years, a large body of research has accumulated on the beneficial effects of infrared light in the range of 600 to 1000 nm. Infrared light can activate mitochondria, which in turn stimulate second messenger systems, DNA transcription, and growth factors.[1,2] As a result, new synapses are formed, circuits regrow, and pluripotent stem cells differentiate into neurons.

Animal studies have shown that infrared photobiomodulation (PBM) may reduce the size and severity of brain injury and stroke, as well as diminish damage and physiological symptoms in depression, posttraumatic stress disorder (PTSD), Parkinson disease, and Alzheimer disease.[1,3-6] Michael Hamblin, PhD, from the Wellman Center for Photomedicine at Massachusetts General Hospital in Boston, a leader in the field, describes PBM as "the use of red or near-infrared light to stimulate, heal, regenerate, and protect tissue that has either been injured, is degenerating, or else is at risk of dying."[1]

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Generally in medicine we shy away from the word "heal" when referring to the brain, and "regenerate" stirs vague recollections of *Frankenstein*. Nevertheless, early findings in mouse models of brain injury and disease have spawned a different sort of monster in the commercial world. The internet is now loaded with companies offering infrared LED helmets or pads for the treatment of traumatic brain injury (TBI) and other brain disorders, often based on exaggerated claims about "healing" the brain. Exorbitant prices in the thousands of dollars are charged for a device that can be made for less than $30. As a result, the public is misled and the potential scientific benefits of infrared light are sullied.

It is time to separate fact from fiction. Yes, infrared light can induce the cellular events described here, reduce the size of stroke injury or TBI in mouse models, and protect neurons from neurotoxins. But is treating a human with a 0.5-W LED the same as treating a mouse? Certainly not! When it comes to infrared light treatment, it is all a matter of getting there: the infrared light must be able to penetrate all the overlying tissue to reach the brain.

Can Infrared Light Reach the Brain?

Can 0.5-W LEDs penetrate human scalp and skull to reach the brain? The answer is "No."[2] My colleague, Larry Morries, DC, and I showed that these LEDs did not even penetrate 2 mm of human skin. In contrast, our laser device, which emits infrared light in the range of 10 to 15 W, was able to effectively penetrate human tissue. We found that 33% of our 10-W infrared laser energy penetrated 2 mm of human skin and delivered from 1.2% to 2.4% of the energy from our device 3 cm into the brain. These data were replicated in a study by Juanita Anders, PhD, and colleagues at the Uniformed Services University of Health Sciences.[7]

The human scalp and skull provide a significant barrier. Infrared light energy needs to be in the range of 0.9 to 15 J/cm^2 at the target tissue to activate mitochondria and other cellular events.[2-3,8-9] Even if a 0.5-W LED only had to penetrate the skull to reach the surface of the brain, it could only deliver 0.0064 J/cm^2, or 1/140th of the minimum energy necessary to induce PBM.[10] No energy would be expected to reach the depths of the brain needed to treat stroke, Parkinson disease, Alzheimer disease, or many brain injuries. Although more than 40% of the incident light from a light source may penetrate mouse skull, only 4.2% penetrates human skull.[8,10]

There is a hairier problem facing LED devices: human hair blocks infrared light. More than 98% of infrared light can be blocked by 2 mm of hair (ie, 9.764 W of a 10-W beam of 810 nm infrared light is

absorbed by human hair).[11] If 98% of the energy from a 0.5-W LED is absorbed by hair, 80% to 90% is absorbed by 2 mm of skin, and 96% of incident energy is attenuated by skull, then claims of neurophysiological benefits of LED-based devices become highly questionable.

Another misconception propagated by companies selling LED-based devices is that multiple LEDs somehow increase light penetration, even though each LED projects light on its own path. For example, 100 0.5-W LEDs do not generate 50 W on the brain, they generate 0.5 W on 100 spots.[11] The argument that light scattering in the brain provides the cumulative value of multiple LEDs also falls apart if nothing can get through the overlying tissues.

Given that a small percentage (<1%) of incident infrared light gets through human scalp and skull, we must question the results of human trials of LEDs. Studies demonstrated small yet almost insignificant positive effects, and the benefits are generally transient.[12] In contrast, our protocol yields persistent and robust clinical changes in patients with TBI, PTSD, and depression.

Treating TBI, PTSD, and Depression with Infrared Light

Our patented multi-Watt Neuro-Luminance approach involves transcranial infrared laser treatment (NILT), and in 2015 we published an initial open-label trial of 10 subjects with mild to moderate TBI.[13] After a course of 10 NILT treatments (20 treatments in a subset of 4 patients), all patients experienced significant clinical improvement of symptoms, including headaches, cognitive problems, sleep disturbances, irritability, and depression. In telephone interviews every 6 months after treatment, patients report sustained improvements.[12]

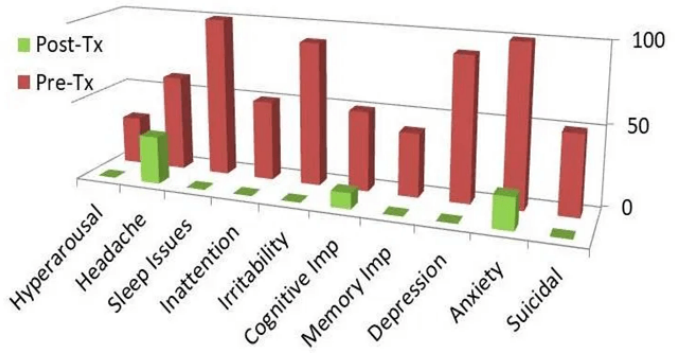

Figure 1. Clinical improvement of symptoms after multi-Watt NILT. Red bars, percentages of patients with symptoms before treatment; green bars, percentages of patients with symptoms after treatment.

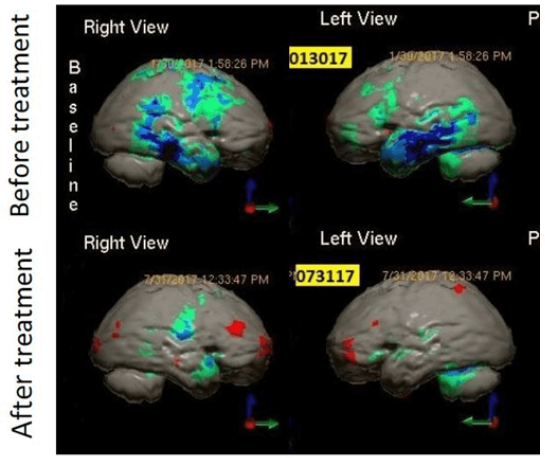

Figure 2. Pre- and posttreatment SPECT scans in patients with TBI after a fall from a truck at freeway speed. Areas of decreased perfusion (function) in green, light blue, and dark blue show improvement after multi-Watt NILT. Color scale based on comparison to a normative database (Segami Corp) in which areas of grey are within 2 standard deviations (SD) of the mean cerebral blood flow of the normative database. Green, 2 to 3 SD below mean; light blue, 3 to 4 SD below mean; dark blue, 4 to 5 SD below mean; red, 2 to 3 SD above mean.

An open-label clinical trial (n=39) of multi-Watt Neuro-Luminance demonstrated effectiveness for depression.[4] Overall, 92% of patients responded and 82% remitted, which is notably better than the response rate for oral antidepressants. Patients saw benefits within 4 treatments, and some achieved resolution of depressive symptoms within 8 treatments. In follow-up telephone interviews, patients report sustained improvements. Similarly, in our unpublished data, using a protocol of 20 treatments, each lasting 24 minutes, over the course of 9 weeks, 20 patients with PTSD treated with multi-Watt NILT experienced reduced hyperarousal, anxiety, sleep disturbance, and nightmares.

LED Photobiomodulation in Comparison

Naeser and colleagues[15] treated 2 patients with TBI daily for approximately 1 hour by applying 3 separate LED cluster heads (2 head; 1 foot). The first patient, who was 7 years post-TBI and had significant postconcussive symptoms, received weekly treatments over the course of 7 months and then daily treatments at home for more than 6 years. The patient experienced transient benefits, and if treatment was stopped, symptoms returned within 2 weeks.[15] The second patient received daily treatments, and in 4 months, most symptoms improved, allowing her to return to work. This patient also noted that symptoms returned if treatments were stopped for more than 1 week.[15]

In an open-label study,[16] 11 patients with TBI and persistent cognitive dysfunction were treated for 18 sessions, each lasting 20 minutes, over the course of 6 weeks. At follow-up, there had been a significant effect on attention, inhibition, verbal learning and memory, and long-delay free recall.[16] The LED treatment led to mild improvement in 3 of 5 cases of depression.

In 12 patients with TBI treated with 220 0.5-W LEDs for 18 sessions, each lasting 20 minutes, over the course of 6 weeks, there was significant improvement in psychological testing results (P =.45).[17] However, the study did not correct for multiple comparisons, instead using parallel paired t-tests, which could exaggerate findings.[18] PTSD has received considerably less attention.[19,20]

Cassano and colleagues[21] described a 5-W laser treatment of 4 patients with depression. In a double-blind, sham-controlled extension of their initial findings, subjects in the treatment group received 16 treatments, each lasting 30 minutes, over the course of 8 weeks.[22] In 13 completers, Hamilton-D-17

scores separated the treatment group from sham controls (mean score, −15.7±4.41 vs −6.1±7.86; *P* =.031). In contrast, in our open-label trial of a 13-W laser, the mean Hamilton-D-17 score decreased from baseline (mean score, 21.48±5.24 to 6.0±5.12; $P = 6.45 \times 10^{-13}$).[23]

Table. Case series, open-label, and double-blind studies of infrared light therapy for TBI, PTSD, and depression

Condition	Modality	Treatment	Persistence	*P* value	Reference
TBI	LED	Daily 1 hour treatments for 7 months	None: symptoms returned after treatment stopped	Case series	15
TBI	LED	Daily 1 hour treatments for 6 weeks	None: symptoms returned after treatment stopped	Case series	16
TBI	LED	18 treatments over the course of 6 weeks, 20 minutes each	Not reported	*P* =.045, not corrected for multiple measures	17
TBI	13-W laser	20 treatments over the course of 9 weeks, 20 minutes each	Persistent to at least 7 years	Case series	13
PTSD	LED	18-20 treatments over the course of 6 weeks, 110 minutes each	None	Not provided	Naeser, unpublished data
PTSD	13-W Laser	20 treatments over the course of 9 weeks, 20 minutes each	Persistent	Preliminary analysis,*P* =.0000067	Henderson and Morries, unpublished data
Depression	5-W Laser	16 treatments over the course of 8 weeks, 30 minutes each	None	*P* =.031	22
Depression	13-W Laser	20 treatments over the course of 9 weeks, 20 minutes each	Persistent to at least 5 years	$P = 6.45 \times 10^{-13}$	23

Alternative Explanation for Clinical Response to LED Brain Treatments

Researchers, along with the human PBM field, need to reconsider the potential mechanisms underlying the meager improvements derived from LED-based devices. The light from LED devices may not

penetrate beyond the skin, but could induce central nervous system benefits via a remote or systemic effect in irradiated skin, dubbed remote photobiomodulation.[24]

Infrared irradiation can have remote or indirect effects on tissue that has not been irradiated. For example, Braverman and colleagues[25] demonstrated this indirect effect by creating matching skin lesions on the left and right dorsum of a rabbit, treating 1 side with infrared light. Both lesions showed accelerated healing relative to nonirradiated controls. Rochkind and colleagues[26] demonstrated that remote PBM could occur in the peripheral nervous system and the central nervous system. After bilateral sciatic nerve crush, 1 side was irradiated with infrared light and the other side was not. Nerves on both sides showed enhanced recovery of function, and the number of anterior horn motor neurons was greater on both sides compared with nonirradiated controls.

Ganeshan and colleagues[27] irradiated the dorsum and hind limbs of a rat with infrared light (670 nm) before injection of a neurotoxin (MPTP) and demonstrated reduced loss of dopaminergic neurons in rodents treated with indirect PBM to the skin compared with untreated controls. Given the overwhelming evidence that low-power LEDs do not penetrate the brain, it is more likely that the benefits of LED-based devices result from an effect mediated by the skin, where most, if not all, of the infrared energy is absorbed. In other words, LED-based devices may be working by remote PBM.

Conclusions

The excitement about the potential of infrared light therapy is not merely that it does not involve taking a pill. There is considerable enthusiasm about its potential to treat conditions such as TBI, dementia, and Parkinson disease. In our excitement, we must not overlook the unique physical limitations of light. Similarly, we must not imbue infrared light with magical powers. Infrared light can only work if it reaches target tissue.

Thus, a sharp divide can be drawn between LED-based treatment technologies, which offer minimal results and may not even reach the brain, and multi-Watt technologies that demonstrably reach the brain and offer lasting clinical benefit. Potentially, infrared light may prove to be effective for numerous neuropsychiatric conditions. However, for infrared light to work on the brain, it must be able to reach the brain.

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