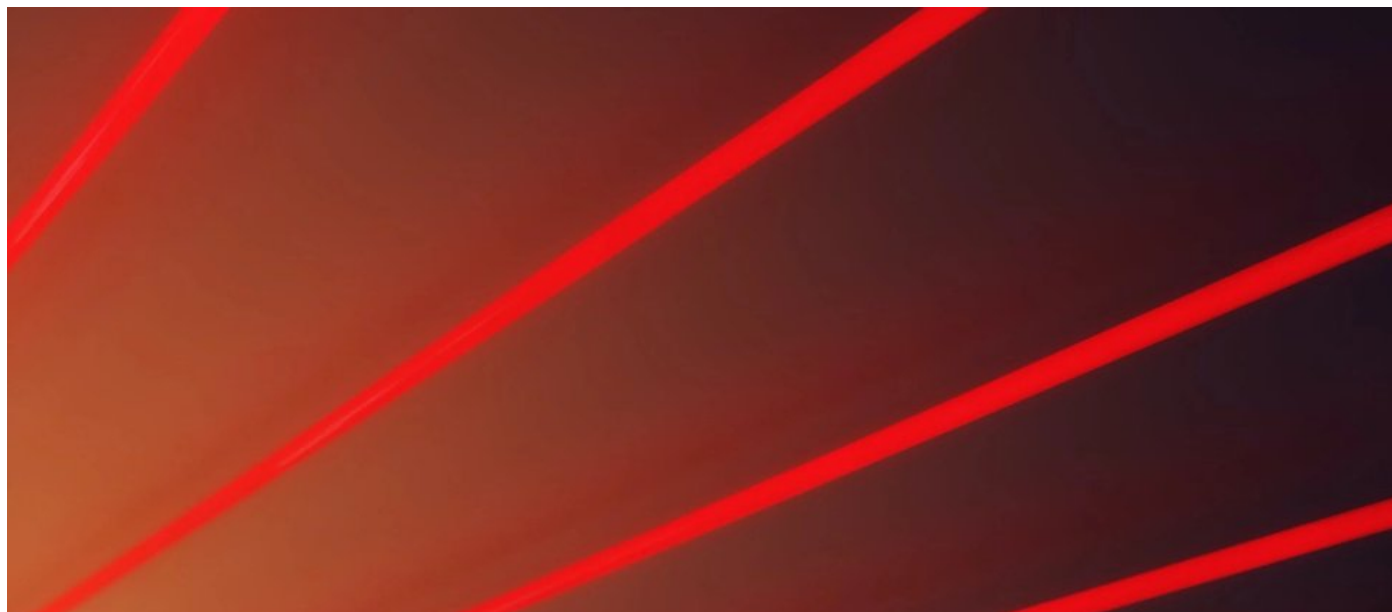


The Hype Around Photobiomodulation



A healthy skepticism in the face of the marketing fanfare is always a good way to protect ourselves from getting conned, even when the latest product getting hyped looks fairly scientific. Skepticism means steering clear of gullibility. That being said, it doesn't mean denying good science, nor should it invite cynicism. It is a balancing act, in constant need of adjustments, and one that can be informed by a better understanding of the realities of scientific research. When we recognize what science can actually deliver, we can adjust our expectations.

I was recently asked about my thoughts on the field of photobiomodulation, specifically as a tool to treat dementia. Photobiomodulation is a technique by which light is used to stimulate living things into healing themselves. It has taken the form of handheld lasers, of helmets full of LED lights, of futuristic tanning beds, even of strange nose clips that shine a light inside the nostril to reach the brain.

Reviewing the literature on each application of photobiomodulation—from smoking cessation to spinal cord injury, from wound healing to age-related

degenerative conditions—would be laborious. Instead, I want to take a bird's-eye view of the hype around photobiomodulation and point out the sobering context in which it exists: exciting findings in cells and animal models rarely lead to applications in humans, and it is all too easy for overeager scientists to fantasize about *how* an intervention might work before it has even been *shown* to work.

Saved by a hair

The year was 1965. Three doctors in the Boston area [published the results of their experiments](#), in which they showed the potential for lasers to treat cancerous tumours. A Hungarian physician by the name of Endre Mester took notice and attempted to reproduce these results. The problem is that his own laser was much less powerful than the Bostonians' and the tumours on his lab rats were not affected. However, serendipity knocked at his door. The skin around the tumours had been shaved to better observe what was going on, and Mester noticed that, following his use of the laser, both hair growth and wound healing were accelerated. He had stumbled upon a finding that would guide his career moving forward.

His laser was not very powerful: it was a low-level laser, of the sort that doesn't burn living tissue, and the potential therapeutic applications of this type of laser became known as either cold laser therapy or low-level laser therapy. The problem is that "low-level" is ambiguous and not particularly scientific, and over the years it was shown that LED lights, like the ones now used in traffic lights and flashlights, could produce similar effects to the cold lasers, so low-level laser therapy was renamed photobiomodulation. The wavelengths typically used for these therapies are in the red and near-infrared part of the light spectrum.

Of course, there's nothing silly about the idea that light influences biology. Our wake-sleep cycles are heavily influenced by light, and our skin makes vitamin D out of cholesterol when it's exposed to ultraviolet light. Our entire

visual system is a complex apparatus dedicated to translating packets of light into information our brain understands. Clearly, the human body—to say nothing of the plants that convert carbon dioxide into sugar with the use of sunlight through photosynthesis—needs and responds to light.

But photobiomodulation or PBM makes therapeutic claims. Websites selling at-home devices or in-clinic treatments can be seen advertising the technology's alleged ability to increase longevity, improve immunity, and help with dementia. The scientific literature is replete with review articles looking at PBM's applications for [stroke rehabilitation](#), the treatment of [depression](#) and [Alzheimer's disease](#), even [the boosting of athletic performance](#) (at the gym and [in the bedroom](#)). Some, believe it or not, speculated it could be used to [treat COVID-19 patients](#).

Most of the studies done on PBM were carried out in laboratory animals. On top of this imposing pile of pre-clinical evidence, there is a sprinkle of human studies, often uncontrolled case reports that are little more than anecdotes. The clinical trials that do exist are very small.

It is appealing to think that the lab mice's improvements when exposed to red light reflects what will happen to us when subjected to the same treatment. But we are not giant mice, and nowhere is this more eye-opening than by looking at the data we have on what happens to the promises of early research findings.

One in ten

Mice are not experimented on for the fun of it. They and other animal models of disease are part of a pipeline that allows researchers to test their understanding of illness with the ultimate aim, often, of getting a new treatment approved. This pipeline stretches from cells in culture flasks to animal models to larger and larger groups of human participants in the three main phases of clinical trials. What looks promising when tested in cells may not hold up in mice, and what still looks favourable in these small critters

may not be efficacious or even safe in humans. It's a gauntlet that needs to be traversed and it causes a lot of attrition.

How much attrition? Perhaps the most thorough survey of this phenomenon was [published in 2014](#) and it looked specifically at pharmaceutical drugs. Its authors found that only about one out of every ten drugs that begin to be tested in humans eventually gets approved. One in ten. Let that sink in. The success rate used to be higher, by their estimates one in five to one in eight, looking at data from the 1960s onwards. There are many reasons for this downtick in our success rate. The low-hanging fruit has already been picked, so it's becoming harder to find drugs that work. Drugs are being compared to a standard of care that itself keeps getting better. And regulators are a bit more careful with regards to safety ever since the 2004 Vioxx recall.

An intervention like a drug or, let's say, a laser or red LED light may appear to work in mice, but the odds of these results holding steady when properly tested in humans are, statistically speaking, not great. This is not the siren song of cynicism, to be clear. Biomedical research is important, but it is hard. Coming to terms with how unlikely preliminary results are to translate into an approved clinical intervention allows us to adjust our expectations to be in line with reality.

Even [a 2016 highly positive review article](#) on PBM's potential use in wound healing concludes with this cautionary note: "most studies on the influences of laser irradiation on wound healing have been performed in mice, rats or ex vivo models [meaning that cells or tissues were taken out of the animal to be experimented on], while few have been performed clinically." Famously, PBM was tested to treat acute stroke in three increasingly larger trials in humans, and in keeping with what is typically seen when false positive results face the music of scientific rigour, the technique went [from working well to only working for a subset of patients to failing in the third trial](#), to the point where this latter experiment had to be prematurely terminated for futility.

"But we understand how photobiomodulation acts at the molecular level," I

hear some of you say. Given that we have a mechanism of action, doesn't this mean that it works?

From A to B

Scientific papers on photobiomodulation are quick to explain exactly how this healing light probably operates on living things. Based on research by Dr. Tiina Karu and her team, PBM is thought to work through the mitochondria. Our cells—and those of animals, plants and fungi—contain tiny structures called mitochondria that generate the energy we need.

Mitochondria have a chain of proteins that juggle electrons, and one of them, cytochrome c oxidase, contains heme and copper that absorb light, especially in the red and infrared part of the light spectrum. So, we shine one such light on living tissue, it gets absorbed by mitochondria's cytochrome c oxidase, and what we get is a veritable biological domino effect that seemingly benefits every part of the organism. The brain gets more blood flow, our cells get more energy, genes and stem cells get activated left and right. It's a chain reaction that has led researchers to look for every potential application of this technology, often portrayed as a cure-all in waiting.

And this is where our second lesson unfurls. Biology has such an impressive cast of molecular characters, it is all too easy for scientists to connect a series of dots between A and B. Our bodies contain [roughly 70,000 unique proteins](#), some being further distinguished by additional modifications.

Finding a plausible molecular chain of events is easy and even encouraged in scientific papers. It is not rare to find an article showing dubious results from an experiment done in six hamsters backed up by multiple paragraphs explaining the precise molecular sequence that might explain these findings.

But even if, in the case of PBM, it is true that certain wavelengths of light activate an enzyme in our mitochondria which has a ripple effect on other molecules, it does not mean that the end result will be clinical improvement. Our body is full of buffers and redundancies to maintain its equilibrium. Just

because some molecules are triggered by a ray of light does not imply that a healing process is afoot.

I remain skeptical, especially of the more outrageous claims of photobiomodulation, and I still don't understand how sunlight does not already provide whatever benefit PBM lights possess. When it comes to using this light to treat the brain, it is still unclear exactly how much of the light applied to the skull or inside the nose reaches the brain, though [experiments agree it is a tiny fraction of the light's output](#). There is still a lack of agreement on the exact wavelength and power that should be used. I will [quote Paul Ingraham](#), whose fantastic website, Pain Science, takes a critical look at pain treatments. "Laser therapy [and here he means photobiomodulation as a whole] is a classic example of premature hype about a futuristic, 'high-tech,' unproven therapy," he writes. "Clinical practice races way ahead of the science, which barely exists, and all the hopes are pinned on vague and unfalsifiable biological plausibility, and research that is rife with fancy-sounding 'mechanism masturbation'—wishful and fanciful speculation about *how* it works rather than focusing on whether or not it actually does." Many studies of PBM are funded by, executed by, and written up by people who own companies that sell these services and by their advisory board members. In and of itself, this is not a reason to toss out their results sight unseen, but it is a conflict of interest and an important one given the paucity of good clinical data supporting this technology.

This rapid commercialization of exciting science that isn't technically ready for primetime has been called scienceploitation, and unfortunately PBM is bathing in it. The move toward using LEDs instead of lasers has been beneficial to this marketing effort: the FDA considers an LED's power level to be below that which constitutes a medical hazard, so [devices using them are not regulated as tightly as those employing more dangerous technologies](#). PBM also occasionally plays footsie [with laser acupuncture](#), a debunked practice that makes use of fictional points on the body to treat all kinds of illnesses, and some of the proponents of PBM can be seen adopting an anti-

pharmaceutical and even [anti-sunscreen](#) attitude that reeks of an appeal to nature. And the idea of shining light inside a body cavity to reach the brain recalls [the dodgy HumanCharger product](#), with at least [one PBM article](#) approvingly citing the criticized research behind this device.

That is not to say that all of PBM's applications are hogwash or that future research will never produce more effective applications of it. But given biomedical research's modest success rate these days and the ease of coming up with a molecular pathway that fits our wishes, we're going to need more than mice studies and a plausible mechanism of action to see photobiomodulation in a more favourable light. A healthy skepticism is needed here, especially when it comes to claims of red light improving dementia.

Take-home message:

- Photobiomodulation is dedicated to the idea that cold lasers or red and near-infrared lights can stimulate the body to heal itself of a variety of diseases
- The vast majority of research into photobiomodulation was done on animals, not humans, and most positive results in lab animals do not lead to approved interventions in humans
- Proponents of photobiomodulation will often cite that we understand how it affects the body at a molecular level, but these kinds of mechanisms are easy to hypothesize and they do not imply that the technology is actually curing anything

[@CrackedScience](#)