Photobiomodulation and Optometric Phototherapy

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Scientists have known since at least the late 1800s that certain wavelengths of light in prescribed doses can be used to heal the tissue.

In the vision care community, light is being used as:

Intense Pulsed Light Therapy (IPL) for dry eye
Red- light treatment of myopia control
Optometric or Syntonic phototherapy for treating visual conditions such as strabismus, amblyopia, and photosensitivity following brain trauma.

Photobiomodulation (PBM) is the current term being used to describe light therapy that is non-thermal and utilizes non-ionizing radiation in the visible and near-infrared spectrum. It was formerly called low-level laser (light) therapy or LLLT.

Visible light being used and studied is primarily long wavelength red light or short-wavelength blue light.

Light's importance for treatment of:

Dry eye

Age-related macular degeneration (AMD)

Post-cataract surgery

Migraine headaches

Cognitive enhancement

Brain injury

Alzheimer's disease

Parkinson's disease

Other neurodegenerative diseases

HISTORY OF PHOTOTHERAPY

The modern use of light in medicine generally is credited as beginning with the work of Niels Ryberg Finsen, a Danish physician

He was awarded the Nobel Prize in Medicine in 1903 for his work using ultraviolet light to treat Lupus.

Publications over the next few years included:

Light and Its Rays as Medicine by Dr Seth Pancoast

The Principles of Light and Color by Edwin Babbitt, MD

In the 1920s, optometrist and physician Harry Riley Spitler

determined that:

Imbalance in the autonomic nervous (ANS) was responsible for many visual conditions

Specific frequencies of light, delivered, through the eyes could be used to rebalance the ANS

And, thereby, correct many visual dysfunctions at their source.

The new science was named ‘‘Syntonics’’

meaning to be responsive and in harmony with the environment

PHOTOBIOMODULATION

In the 1960s it was found that:

Treatment with a weak ruby laser could improve wound healing

The treatment was maligned for many years until the mechanism was made known through the work of Tiina Karu in Russia.

Tiina Karu identified *cytochrome c oxidase* in the mitochondrial respiratory chain as a primary chromophore

She showed that a brief exposure to light could have an effect on the organism that lasted for hours, days, or weeks.

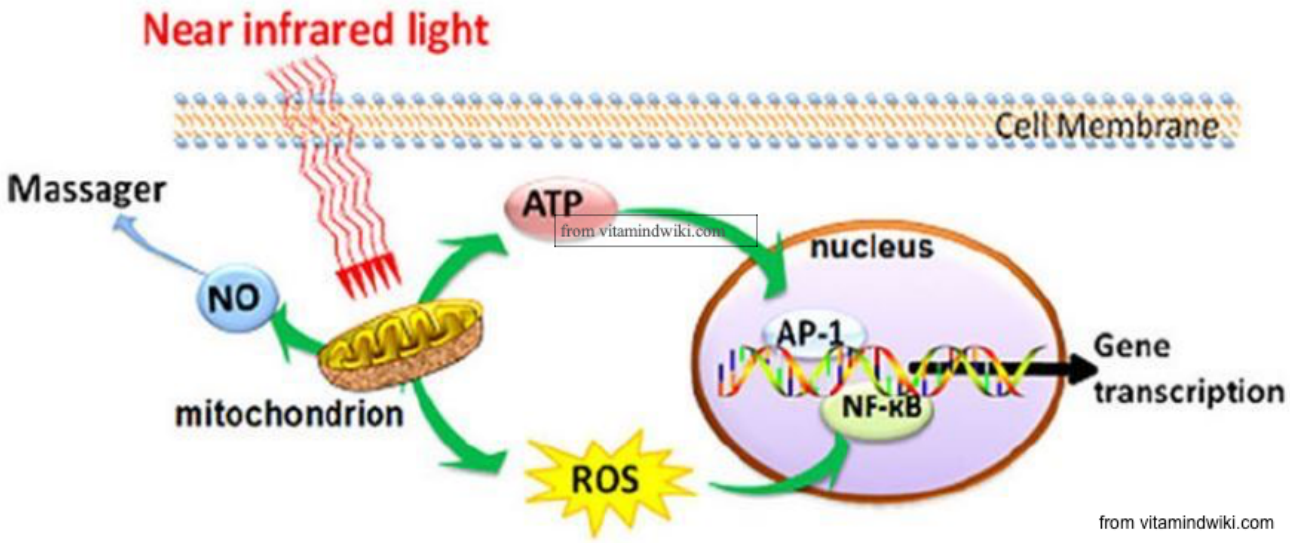
Under stress, as from disease conditions, the mitochondria produce too much nitric oxide which attaches to cytochrome c oxidase molecules

Cytochrome c oxidase blocks adenosine triphosphate (ATP) synthase from producing ATP

Without ATP, the cell cannot carry out its normal growth and repair

Red and near-infrared light cause the cytochrome c oxidase molecules to release the nitric oxide, allowing the resumption of ATP production

Research has shown measurable improved cellular function within minutes to hours of the application of photobiomodulation



For PBM to be successful, a light source is placed close to the eyes or in contact with the skin

This allows the light to penetrate the tissue and interact with chromophores in cells >> photophysical and photochemical changes. These changes:

accelerate wound healing

increase circulation

reduce acute inflammation

mitigate acute and chronic pain

help restore normal cellular function.

Red and near-infrared (650–940 nm) light penetrates most deeply into human tissue

Interest is increasing in the use of violet, green, and blue light (430–550 nm) frequencies to also effect positive changes in human physiology

THE NON-VISUAL OCULAR PATHWAY

A third light-sensitive receptor in the retina was identified in 2002
Known as intrinsically photosensitive retinal ganglion cells (ipRGCs).

These retinal ganglion cells are:
Associated with the photopigment melanopsin
Are maximally sensitive to blue light

They number only about 2% of the retinal ganglion cells

Fibers from these cells bypass the visual cortex and travel to the suprachiasmatic nucleus (SCN) of the hypothalamus

Coordinate the body's circadian rhythm

The ipRGCs and their connection to the hypothalamus provides a model for the treatment efficacy of phototherapy

Sets up the introduction of light frequencies through the eyes as a way to institute changes in the endocrine system.

CLINICAL PRACTICE

Optometric (Syntonic) phototherapy may be considered a form of photobiomodulation.

How our light sources and filters differ from what is now mostly LED application is something we may want to ask those creating the newest devices

NEUROPROTECTION and AGE-RELATED MACULAR DEGENERATION

The retina is vulnerable to mitochondrial dysfunction, especially with increasing age

Retinal photoreceptors and ganglion cells contain a high density of mitochondria

This makes them an excellent target for the reduced cell death and mitigation of oxidative stress offered by photobiomodulation

Janis Eells, PhD – an early researcher studying the effect of near-infrared light therapy for retinal healing

Early studies centered on the loss of vision in laboratory mice following methyl alcohol toxicity

The mice were subjected to near-infrared light before being given a toxic dose of methanol
The mice exposed to the light did not demonstrate the loss of vision and retinal damage seen in the untreated mice

PHOTORECEPTOR NEUROPROTECTION

Nora Heinig of the Technische Universitat (TU) Dresden, School of Medicine

Primarily looking at the neuroprotective effects of 670 nm red light and 810 nm near-infrared light on blue light-damaged murine primary photoreceptors

They noted:
Improvement in mitochondrial respiration
Reduced retinal inflammation
Reduced mitochondrial-induced apoptosis.

They also referenced earlier work showing that near-infrared light may:
Reduce photoreceptor death by 70%
Reduce drusen volume
Can lower intraocular pressure for as long as several months.

In 2016, Graham Merry, MBBS, showed that photobiomodulation also reduced drusen volume
While improving visual acuity and contrast sensitivity in dry age-related macular degeneration (ARMD)

More recently, Samuel Markowitz, MD, and colleagues led a controlled study on the use of red-light therapy for dry ARMD

- Significant improvement in
  - contrast sensitivity
  - drusen volume
  - central drusen thickness
- No adverse effects being reported in the treatment group

LumiThera's Valeda Light Delivery System
Uses photobiomodulation to treat eye disease

Still investigational in the United States,
Approved in the European Union for the treatment of ocular damage and disease

Including inhibition of inflammatory mediators, edema, drusen deposition, improvement of wound healing following ocular trauma or surgery and

Increase in visual acuity and contrast sensitivity in patients with degenerative diseases such as dry AMD

Treatments are delivered in a series of nine sessions per eye over 3 weeks and each treatment session lasts less than 5 minutes per eye.

MEIBOMIAN GLAND DYSFUNCTION AND DRY EYE

Eye doctors have two choices of light therapy for treating inflammatory eye disease

IPL uses light but the light is converted to heat with the chosen wavelengths selectively destroying blood vessels by targeting chromophores within the blood vessels

PBM is non- thermal and involves placing a mask over the face through which the light therapy is released

Marco Equinox LLLT device

Marco Equinox Low-Level Light Therapy device

The mask covers the patient's forehead, entire eye area, and cheekbones

The *blue light mask* is used to kill bacteria such as in Staphylococcal blepharitis
After delivery of the light energy, porphyrin molecules on the cell membrane absorb the blue light > generating free radicals that disrupt the cell wall of some gram-positive bacteria > leading to cell death

Cells have a weak defense against the oxygen-induced damage
Treatment is highly effective for dry eye conditions such as: blepharitis, meibomian gland dysfunction, chalazion or stye.

With few side effects, PBM offers a safer and less invasive alternative to pharmaceuticals and surgical interventions.

MYOPIA AND RED-LIGHT THERAPY

Slowing myopia progression has become important
Even low levels of myopia increase the risk for glaucoma, macular degeneration, and retinal detachment

Mechanisms for red light suppressing myopia progression suggest that narrow band long wavelength light promotes hyperopia by retarding axial elongation, decreasing elongation of the vitreous chamber, and increasing choroidal thickness

Bright light suppresses form-deprivation myopia development by activating dopamine D1 receptor signaling in the retina

In 2022 alone, a number of studies demonstrated positive effects of red-light therapy in reducing myopia, reducing axial length, and being well-tolerated with no adverse effects.

Yu Jiang and colleagues used a home-based desktop light therapy device to administer red light of 650 nm wavelength at an illuminance level of approximately 1600 lux and a power of 0.29 mW for a 4-mm pupil.

Treatment was done under parental supervision for 3 minutes per session, twice daily with a minimum interval of 4 hours between sessions.
The treatment was administered 5 days per week.

Subjects in the experimental group had far less myopic progression and axial length change than the control group

They reported a mean spherical equivalent refraction change over 6 months of -0.2D, and average axial length change of 0.13 mm in the treatment group versus a refraction change of -0.79D and axial length growth of 0.38 mm in the control group

Results of a 6-month follow-up showed additional positive results
16% of subjects had reduced myopia
25% showed reductions in axial length
The therapy was well-tolerated with no adverse effects being reported by test subjects

Jing Dong and colleagues administered repeated low-level red-light therapy (RLRL)to a group of Chinese children
Used a desktop red- light device with the experimental group receiving 100% light power and the sham group receiving 10% of the device's power.

Treatment was done at home, and they followed a similar schedule of 3-minute sessions twice daily with an interval of at least 4 hours between sessions.

Cycloplegic refraction and axial length (AL) were measured at baseline and 6 months

Children in the treatment group had less myopia progression and axial elongation compared to the sham control group

At the final visit, distance visual loss was statistically significantly greater for children with myopia in the sham device group than for those in the red-light therapy group

Mean spherical equivalent refraction change over 6 months was 0.06D in the treatment group and -0.11D in the sham device control group

Average AL growth was less 0.02 mm in the treatment group compared with 0.13 mm in the sham control group.

Recognized treatments for myopia including
low-dose atropine
orthokeratology
defocus-incorporated multiple segment (DIMS) spectacle lenses

These are 30% to 60% effective in delaying the onset of or progression of myopia
BUT they are not strong enough to restrain AL growth

PBM therapy modestly decreases AL for myopia control

Red-light irradiation was found to induce hyperopia

Red-light therapy may be a powerful tool in myopia prevention and control

Red light may be a safe treatment given its protective effect on both the cornea and retina.

The effects of light wavelength, illuminance, and contrast on the progression of myopia

Retinal dopamine secretion is affected by light intensity and different light wavelengths
Related to the known effect of focus difference between shorter and longer wavelengths called *longitudinal chromatic aberration theory*

Investigation of the efficacy and safety of 650 nm low-level red light for myopia control in children

The median 6-month change in AL was -0.06 for the treatment group and 0.14 mm for the control group (P. < 0.001)

The median 6-month spherical equivalent refraction was 0.125D for the treatment group and -0.25 for the control group (P. <.001).

Conclusion

650 nm low-level red light was an effective and safe treatment
It significantly slowed myopia progression in the children treated
It reversed myopia progression in over half the children treated
There were no adverse effects observed

GLAUCOMA AND NEUROPROTECTION

Researchers would like to find treatments that are less invasive or with fewer side effects than current surgical and drug treatments

Photobiomodulation is one therapy being studied as a way to delay glaucoma by slowing down retinal ganglion cell death.

PBM's role in targeting mitochondria may offer protection and delay the onset of glaucoma

PBM may stimulate neural progenitor cells
Leading to a role in slowing down retinal ganglion cell death
Or in part regenerating tissue damaged by glaucoma

A current clinical trial, ClinicalTrials.gov Identifier NCT05309811, is investigating the effect of repeated low-level red-light therapy (RLRL) on existing visual field damage in primary open-angle glaucoma patients

They hope to show that RLRL's ability to improve circulation will have a positive effect on the possible ischemic mechanism of primary open-angle glaucoma and reverse weakened visual function

AMBLYOPIA

Adolescent/adult patients with amblyopia from 20/400 to 20/30
Treated for 30 seconds, 3-4x per week for 2 weeks with 780 nm light

Control patients showed no improvement in visual acuity

Treated patients showed significant improvement in visual acuity

AMETROPIA

90% showed an average acuity increase of three lines

89% of those with strabismus improved an average of 2.7 lines

The beneficial effect was retained for at least 6 months

The exact mechanism of the treatment effect is unknown

- Speculate that increased cellular metabolism and inter-neuronal communication via promotion of synaptogenesis may be responsible for the improvement in visual acuity

MIGRAINE HEADACHE AND PAIN REDUCTION

Exposing migraine sufferers to a narrow band of green light was found to significantly reduce photophobia and headache severity

Rami Burstein, PhD, of the Harvard Brain Science Initiative 2017

Migraine photophobia and experience with color may originate in cone-driven retinal pathways > then fine-tuned in relay thalamic neurons outside the main visual pathway and preserved by the cortex

Allay Lamp and Hooga sell a green light lamp that produces the narrow band of green light found to reduce migraine headache sensitivity

Recommend it to be the only light source in the room to be most effective

FIBROMYALGIA

Padma Gulur, MBBS, reported that 34 fibromyalgia patients were assigned to wearing either green, blue, or clear lenses for 4 hours per day for 2 weeks. (The American Society of Anesthesiologists 2022)

Those wearing the green lenses reduced their reliance on opioids

Four times more likely to report less pain-related anxiety associated with their fibromyalgia

They did not want to give up their green lenses at the end of the study

BRAIN INJURY AND PHOTOBIOMODULATION

Double-blind study on the use of blue light treatment

Test subjects received 30- minute pulses of blue light each morning

Control subjects received pulses of amber light

Test subjects showed significant improvements in:
Sleep timing

Daytime fatigue

Executive functioning

MRIs showed increased volume of the posterior thalamus (pulvinar)

Recent review and meta-analysis of TBI with in vivo mammalian models

Analysis favored light of 665 nm and 810 nm with no differences found between pulsed or continuous wave light delivery

Supports antiapoptotic, anti-inflammatory, and pro-proliferative effects, along with modulation of cellular metabolism

SUMMARY

Modulated light to treat visual and systemic conditions now is considered a safe and effective tool.

Research has changed its mission from if light can heal to how light stimulates healing.

Initial research concentrated on the effect of modulated light in mitochondria and the cytochrome c oxidase molecule with its ability to allow the release of nitric oxide and assist the cells in increasing ATP production.

Research is expanding to include many other positive effects for light as medicine.

ipRGC's and their connection to hypothalamus support the use of light in the maintenance of health

Autonomic system balance validates the use of light through the eyes to treat organic and functional vision disorders.

The vision care community can now use devices that deliver modulated light through the eyes for:

Macular degeneration

Dry eye

Myopia Control

Amblyopia

Migraine Headaches

Sequelae of Brain Injury

Future Light therapy for:

Alzheimer's disease

Parkinson's disease

Other neurodegenerative diseases

Prevent or slow ocular conditions resistant to current surgical/drug interventions

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