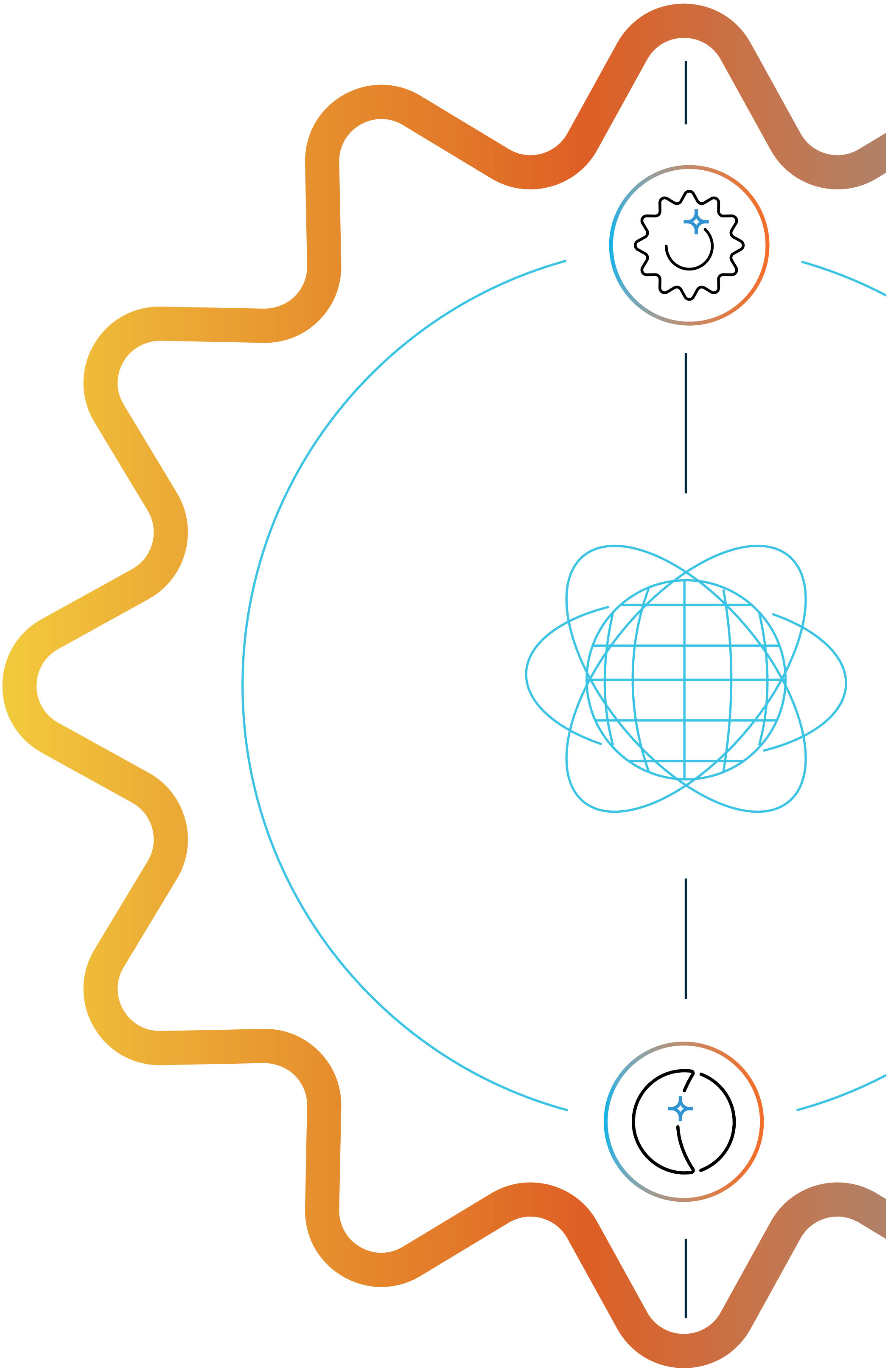


THE SCIENCE BEHIND

01

THE DISCOVERY OF AN EXCITING BLUE LIGHT SENSITIVE PHOTORECEPTOR – MELANOPSIN

After 150 years of research on human eyes, scientists have managed to explain how we are able to see – through two photoreceptors located in our eyes. Those are the rods (black & white vision) and the cones (color vision).
Up until the beginning of the 21st century, the question of how light is able to regulate circadian rhythms of humans has been unanswered.
After conducting clinical studies both in Harvard and Oxford, scientists have showed that, even without rods and cones, humans are able to regulate their biological rhythms. That led to the discovery in 1998 of a new photopigment (melanopsin), located also in the human eye, which is maximally sensitive to blue light and is responsible for the regulations of circadian rhythms.

02

THE AMAZING EFFECT OF BLUE LIGHT ON HUMANS

There are numerous clinical studies conducted to examine the positive effect of blue light on humans for optimizing biological rhythm. From 1995 until 2001 Dr. George C. Brainard and his colleagues have tested more than 70 people in around 700 experiments to evaluate which is the strongest wavelength for melatonin suppression. Their experiments concluded that this is the blue wavelength in the span 459-485nm. As a result, melatonin suppression helps people sync their biological rhythms and thus, increase their overall wellbeing.

03

SUMMARIES OF SCIENTIFIC STUDIES ON THE EFFECT OF BLUE LIGHT

“High Sensitivity of the Human Circadian Melatonin Rhythm to Resetting by Short Wavelength Light”

Steven Lockley, George Brainard, Charles Czeisler , 2003

Outcome

“Exposure to 6.5 h of monochromatic light at 460 nm induces a two-fold greater circadian phase delay than 6.5 h of 555 nm monochromatic light of equal photon density. Similarly, 460 nm monochromatic light causes twice the amount of melatonin suppression compared to 555 nm monochromatic light, and is dependent on the duration of exposure in addition to wavelength. These studies demonstrate that the peak of sensitivity of the human circadian pacemaker to light is blue-shifted”

“Light therapy for seasonal affective disorder with blue narrow-band light-emitting diodes (LEDs).”

Glickman G., Byrne B., Pineda C., Brainard G., 2005

Outcome

A comparison between the use of blue 468nm light against red 654nm light for treating Seasonal Affective Disorder (SAD) was conducted. The results show that the short wavelength blue light treatment decreased the SAD symptoms significantly more than the dimmer red light condition.

“Blue light from light-emitting diodes elicits a dose-dependent suppression of melatonin in humans.”

West K, Jablonski, M., Brainard G., 2011

Outcome

A comparison of mean melatonin suppression with 4,000 K broadband white fluorescent light, currently used in most general lighting fixtures, suggests that narrow bandwidth blue LED light may be stronger than 4,000 K white fluorescent light for suppressing melatonin and enhancing alertness.

“Blue light improves cognitive performance”

S. Lehrl, K. Gerstmeyer, J. H. Jacob, H. Frieling, A. W. Henkel, R. Meyrer, J. Wiltfang, J. Kornhuber, S. Bleich, 2007

Outcome

A longitudinal study in 44 adults has shown that a significant increase in alertness and speed of information processing could be achieved by blue light as compared to normal light.

04

AYO LIGHT PROPERTIES

The blue light behind AYO is with an approx. wavelength of 475 nm, with an approx. light irradiance of 300 μW/cm^2 projected on the eye and is UV and Infrared light free. AYO light has been carefully selected and tested by an independent body. Furthermore, a comparison between AYO light and the light behind the best-researched and developed appliance amongst the Circadian Rhythm products - Philips GoLite has been made. The following conclusions have been derived from the comparison, which show a clear advantage of AYO over one of the best-performing light therapy devices currently on the market.

1. According to the international eye safety regulations and guidelines EN62471, the light properties of AYO are operating outside any thermal hazard or blue light hazard and are completely safe for the user.

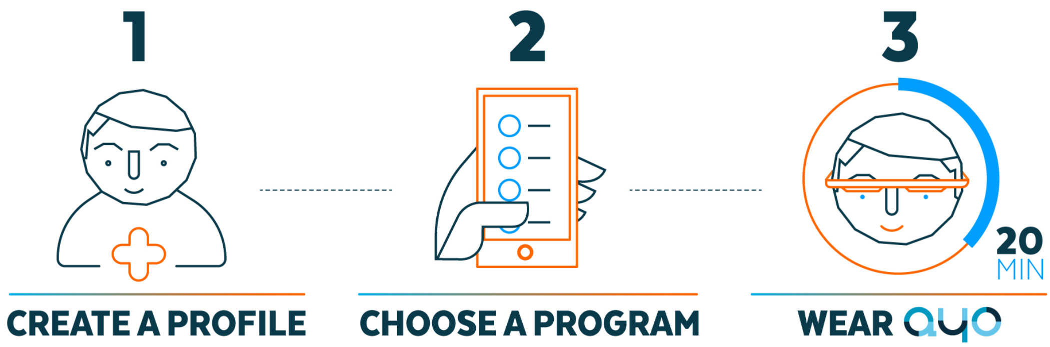
2. Compared to Philips GoLite, AYO has the same light irradiance levels of approximately 300 μW/cm2 but, at the same time, emits 5 times less glare, making it easy on the user's eyes and avoiding irritation.

3. AYO's proprietary technology prevents misuse of the device and ensures proper handling and maximum results, making it the safest and most effective light treatment device on the market.

Conclusion
AYO is independently tested and certified device which is completely safe for the eyes.

05

HOW AYO WORKS



AYO is simple to set up and use - after the user creates a user profile in the AYO app based on his sleep habits and lifestyle preferences, our sophisticated algorithms perform an in-depth analysis calculating critical points for the user's sleep/wake routine and activity levels.

By wearing AYO for only 20 minutes a day, the clinically-backed AYO light can help the user wake up easier while feeling more energized as well as alleviate jet lag or make the user more active in the dark and evening hours, depending on the program the person chooses.

Due to the innovative and user-friendly design, the users can use AYO while brushing their teeth, making breakfast, watching TV, reading the newspaper or checking their emails - it does not distract their eyesight in any way.

AYO LIGHT TREATMENT

AYO uses advanced light treatment to stimulate specialized receptor cells in your eyes

SCN – MASTER “BODY CLOCK”

Activated cells send signals to the area of the brain called Suprachiasmatic Nucleus - biological master clock, optimizing circadian rhythm

EYES - IPRGC

The AYO Light enters the eyes and special cells in the eye called photosensitive Retinal Ganglion Cells are activated stimulating protein called Melanopsin

CIRCADIAN RHYTHM

Circadian rhythm is being adjusted and hormone levels (e.g. melatonin, cortisol, adrenalin, serotonin, etc.) as well as timing are improved

SAFE AND NATURAL

AYO light is absolutely safe and natural way to optimize your body clock. AYO light uses completely natural mechanisms mimicking the sun but without the harmful UV and infrared light. It is based on tested and well-proven technology.

06

SOURCES

The links below are from the aforementioned clinical studies showing the importance of blue light and overall light therapy on the human circadian system.

Melanopsin
http://www.ncbi.nlm.nih.gov/pubmed/18054803

Effects of blue light on humans
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2831986/

Blue light has a stronger effect than green
http://press.endocrine.org/doi/10.1210/jc.2003-030570

Effect of Blue light against red light to treat depression/SAD
http://www.ncbi.nlm.nih.gov/pubmed/16165105

Blue light to stimulate the emotional brain processing
http://www.ncbi.nlm.nih.gov/pubmed/20974959

07

ADDITIONAL RELEVANT LITERATURE

The articles and summaries below explain further the biological effect of light on humans and how the circadian system works. They include results from clinical trials proving the beneficial effect of light on humans used for a specific time and at a specific time during the day.

01. Human Phase Response Curve to Intermittent Blue Light using a Commercially Available Device, 2012

Study on the circadian response to exposure to a commercial blue light device using a intermittent schedule of therapy.

Experiment:

- 57 healthy, young subjects (37 generating sufficient data)
- Subjects participated in two 5 day laboratory sessions, 1 week apart, and intermittent by three days of free-running schedule
- A commercially available blue LED light box (goLITE, 60 LEDS, 11.2 X 6.6 cm, =450-500 nm, max ~ 467 nm, ~200 μW cm^-2, ~185 lux)

Results:

- goLITE was capable of inducing a daily shift of the circadian rhythm ~1 h delay and ~1.5 h advance (probably lower, seeing the PRC below), through daily treatment over a 1.25 h window (75 min therapy as 2x 30 min light pulses with a 15 min break)

02. Handbook of Experimental Pharmacology - Circadian Clocks, 2013

Chapter "Light and the circadian clock"

Experiment:

- Zeitnehmers are feedbacks that are both input and output of the circadian system.
- The SCN's entrainment mechanism involves several zeitnehmer loops, on the molecular, the physiological and the behavioural level.
- Sleep itself is also an important behavioural zeitnehmer loop, because it influences the daily light profiles
- Circadian clocks have evolved to produce an internal day representing the external day. This is different to evolving a specific intrinsic free-running period (τ). A steady-state in artificial constant conditions can only be reliably assessed when measured over several days and thus represents the average internal day that the circadian system produces under a given condition.
- τ is subject to the influence of many factors—beyond DD or LL (of different intensities)—and many of these (e.g. wheel running) will affect different zeitnehmers within the sys-

tem and thereby change τ. While this average internal day (τ) is not reliable to predict entrainment under all conditions, we must presume that every circadian clock produces its individual internal day based on genetic background. The internal day indeed forms the basis for entrainment, but the genetic background of an organism/individual will also influence many other aspects of the circadian machinery—from inputs via zeitnehmers to outputs. The difficulty of this concept is that the length of an individual clock's internal day cannot be measured experimentally since the entraining mechanisms will also be active in constant conditions (e.g. will be the influenced by zeitnehmers) and thereby change . Thus, the length of an internal day can only be assessed theoretically.

- Light remains the most dominant zeitgeber
- Chronotype is influenced by:
- Genetic factors (e.g. CLOCK genes)
- Development (severe delay in adolescence, largely based on biological factors)
- Light exposure
- An experiment involving thousands of subjects in Germany, a country spanning nine latitudinal degrees, suggests that entrainment of the human circadian clock depends on sun time and not on local (social) time.
- Social jetlag is the discrepancy between internal and external time
- The term social jetlag is based on the observation that sleep timing between workdays and free days resembles the situation of travelling across several time zones to the West on Friday evenings and 'flying' back on Monday mornings
- In travel-induced jetlag, these complaints are transient until the circadian clock has re-entrained to the light-dark cycle at the destiny. In contrast, social jetlag is a chronic phenomenon, lasting throughout an individual's working life.
- As to be expected for a day-active species, dawn appears to be more important than dusk for human entrainment (except in short summer nights).
- Both sleep per se (i.e. closing our lids and rolling up our eye balls) and bedroom behavior (retreating into darkness) are becoming the most important dark-signals that entrain the human clock.
- Thus, zeitnehmers potentially become more important to human entrainment than zeitgebers.

03. Controlling Light-Dark Exposure Patterns rather than Sleep Schedules Determines Circadian Phase, 2013

Experiment:

- Circadian phase changes associated with two different light-dark exposures patterns were examined, one that was congruent with a phase advanced sleep schedule and one that was incongruent with an advanced schedule.
- 21 adult subjects (mean age ±standard deviation =22.5 ±3.9 years; 11 women)
- 12 day study, 5 baseline days
- After the 5 baseline days, participants were all given individualized, fixed,90-minute advanced sleep schedules for 7 days.
- Two randomly assigned groups were created:
    - An advance group with a light-dark exposure prescription designed to advance circadian phase
        - Two morning hours of short-wavelength (blue) light (λmax = 476 ± 1nm, full-width-half-maximum = 20 nm) exposure
        - Three evening hours of light restriction (orange-filtered light, λ < 525 nm = 0)
    - A delay group with light-dark exposure prescription designed to delay circadian phase
        - The same blue light for three hours in the evening
        - Light restriction for two hours in the morning
- Participants led their normal lives while wearing a calibrated wrist-worn light exposure and activity monitor.

Results:

- After seven days on the 90-minute advanced sleep schedule, circadian phase advanced 132 ±19 minutes for the advance group and delayed 59 ±7.5 minutes for the delay group.

Controlling the light-dark exposure pattern shifts circadian phase in the expected direction irrespective of the fixed advanced sleep schedule.

04. A Randomized Controlled Trial with Bright Light and Melatonin for Delayed Sleep Phase Disorder: Effects on Subjective and Objective Sleep, 2013

Experiment:

- 40 adolescents and young adults (16-25 years) diagnosed with Delayed Sleep Phase Disorder (DSPD)
- Every subject received a two-week DPSD treatment
- Four treatment groups were formed:
- Dim light and placebo capsules (12 h after awakening, but not before 8 pm)

- Bright light (10 000 lux at wake-up) and placebo capsules (idem)
- Dim light and melatonin capsules (idem)
- Bright light (idem) and melatonin capsules (idem)

- In a follow-up study, participants were re-randomized to receive either, for 3 months:
    - Treatment with the combination of bright light
    - Or no treatment at all
- The main end points were sleep as assessed by sleep diaries and actigraphy recordings and circadian phase as assessed by salivary dim light melatonin onset (DLMO).

Results:

- In all four two-week treatment groups, circadian rhythms were advanced (for detailed results, see table 2 on pg. 79): 1 h advance of bed time, 2 h advance of rise time and 2 h advance of DLMO.
- At three-month follow-up, only the treatment group had maintained an advanced sleep phase.
- Sleep duration had returned to baseline levels in both three-month groups.

05. The Stimulating Effect of Bright Light on Physical Performance Depends on Internal Time, 2012

Experiment:

- 43 healthy, entrained subjects.
- Chronotype of all subjects was measured using the MCTQ and subjects were divided in an "earlier" group, subjects with a more delayed circadian rhythm thus the experiment was earlier in their internal time, and a "later" group, subjects with a more advanced circadian rhythm this th experiment was later in their internal time.
- Subjects were randomly assigned to a dim-light (DL) 230lx or bright-light (BL) 4420lx session.
- Subjects would receive 2h of either BL or DL, the final 40m being a physical performance test.
- After one week subjects participated in a second session.

Results:

- Physical performance peaks late afternoon.
- Bright light exposure advanced subjects their internal time, bringing it more closely to the performance peak. The BL group therefore performed better at the test than the DL group.
- The "later" group exposed to BL had a greater increase in performance compared to the DL group then the "earlier" group exposed to BL. This indicates that when your internal time is closer to the performance peak, the effect of BL is greater.

07

ADDITIONAL READING LIST:

- / A Phase Response Curve to Single Bright Light Pulses in Human Subjects, 2003
- / Human Phase Response Curve to a Single 6.5h Pulse of Short-Wavelength
- / Human Responses to Bright Light of Different Durations, 2012
- / Phase-Shifting Response to Light in Older Adults, 2013
- / A Train of Blue Light Pulses delivered through Closed Eyelids Suppresses Melatonin and Phase Shifts the Human Circadian System, 2013
- / Two Hours of Evening Light Produces Significant Circadian Phase Delay Shifts in Older Adults, 2013
- / Objective Measures of Sleep and Dim Light Melatonin Onset in Adolescents and Young Adults with Delayed Sleep Phase Disorder Compared to Healthy Controls, 2013
- / Entrainment of the Human Circadian Clock to the Natural Light-Dark Cycle, 2013
- / Light level and duration of exposure determine the impact of self-luminous tablets on melatonin suppression, 2013
- / Effects of Artificial Dawn and Morning Blue Light on Daytime Cognitive Performance, Well-being, Cortisol and Melatonin Levels, 2013

07

- / Effects of a Chronic Reduction of Short-Wavelength Light Input on Melatonin and Sleep Patterns in Humans: Evidence for Adaptation, 2014
- / Home Lighting Before Usual Bedtime Impacts Circadian Timing: A Field Study, 2014
- / Optimal Schedules of Light Exposure for Rapidly Correcting Circadian Misalignment, 2014
- / Social Jetlag and Obesity, 2012
- / Blue-enriched office light competes with natural light as a zeitgeber, 2011
- / The Influence of Internal Time, Time Awake, and Sleep Duration on Cognitive Performance in Shiftworkers, 2012
- / Efficacy of a Sequence of Intermittent Bright Light Pulses, 2004

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