

# Chronotherapeutics: Light Therapy and Beyond

Michael Terman, Ph.D.



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- My content will include reference to commercial products; however, generic and alternative products will be discussed whenever possible.
- All products have been evaluated in peer-reviewed grants or publications.

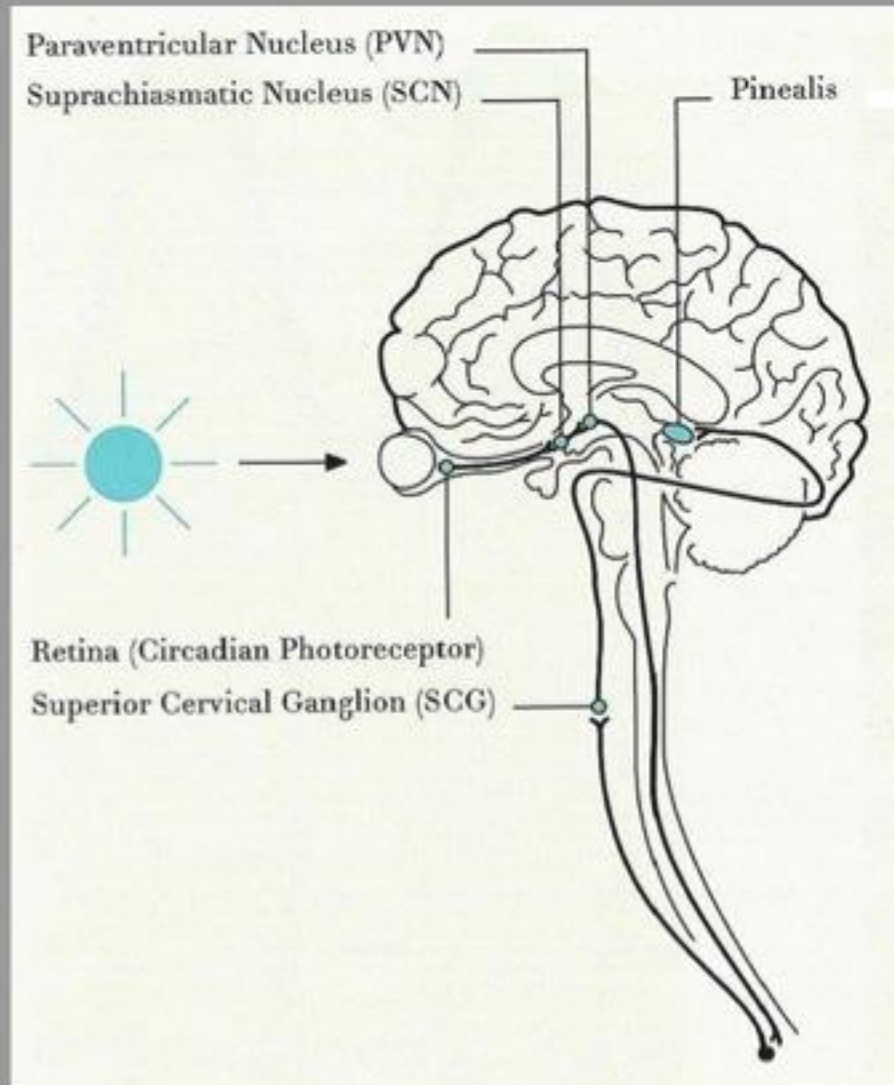
# What is chronotherapy?

A set of treatments – primarily for **unipolar and bipolar depression**, and **sleep phase disorders** – that use one or more of the following, anchored to the patient's circadian rhythm phase:

- Light therapy: bright light or twilight simulation
- Light protection (dark therapy)
- Melatonin administration
- Wake therapy (sleep deprivation)
- Sleep phase advance

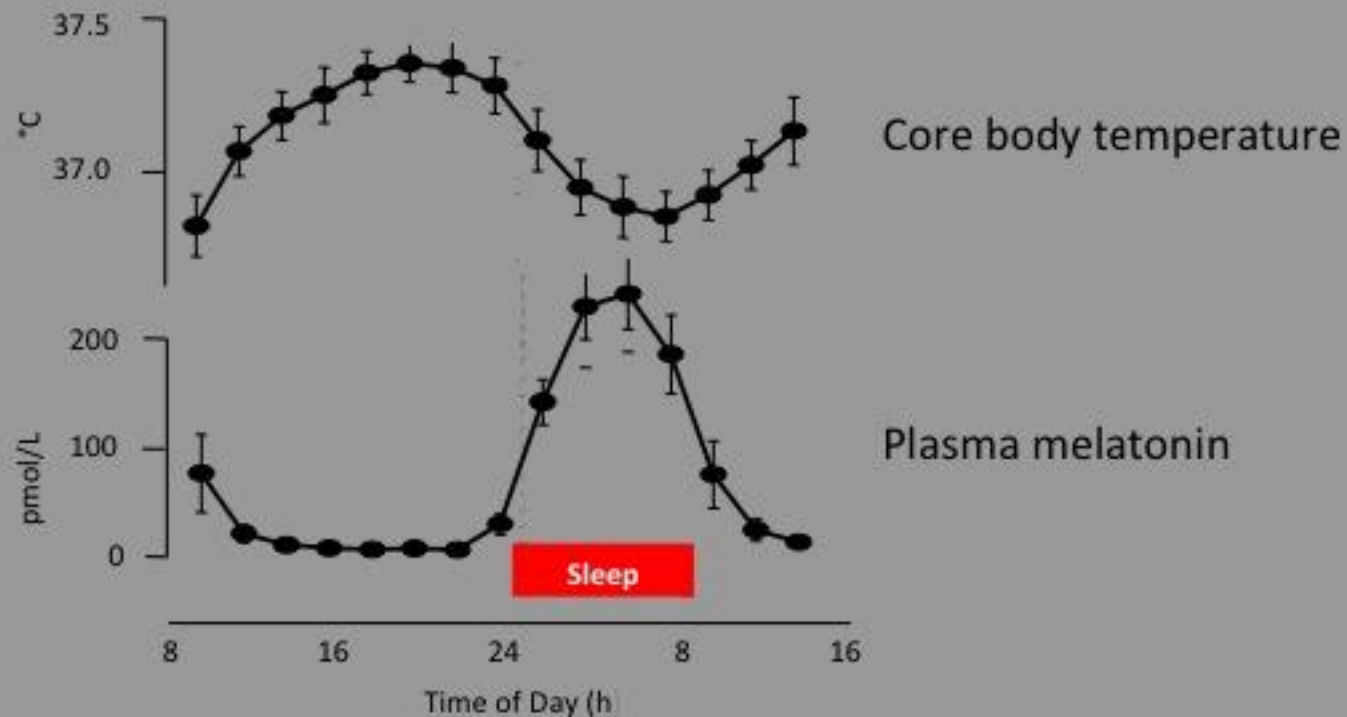
*In the works:* mania, ADHD, OCD, bulimia, dementia, jet lag, shift work, degrees of blindness

# The Circadian Timing System



Wirz-Justice A (2002) The physiology of time. In Décosterd J-G, Rahm P (Eds.): Physiological Architecture, Basel, Birkhäuser. Pp. 147-151.

# Circadian rhythms in synchrony with sleep



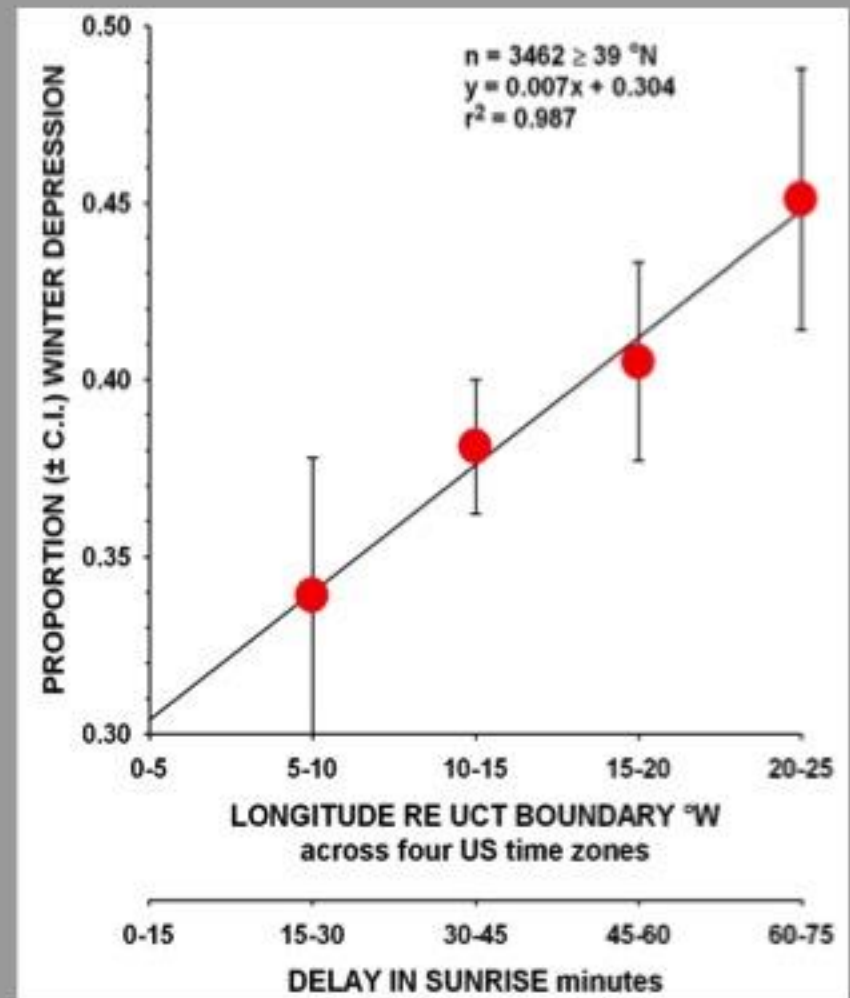
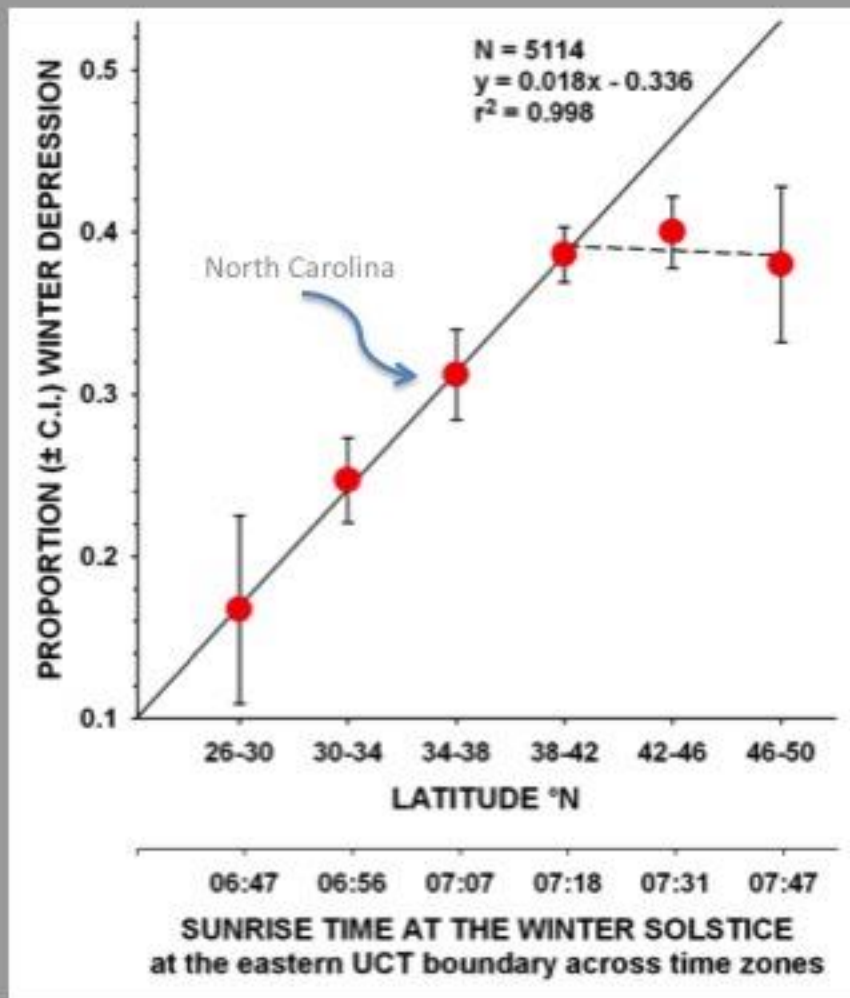
# Recommended\* light box configuration



- Broad field of illumination
- Moderate color temperature (4500K)
- 10,000 lux max
- Directed from above the line of sight
- Polycarbonate UVR filter
- Smooth diffuser
- Tilt- and height-adjustable

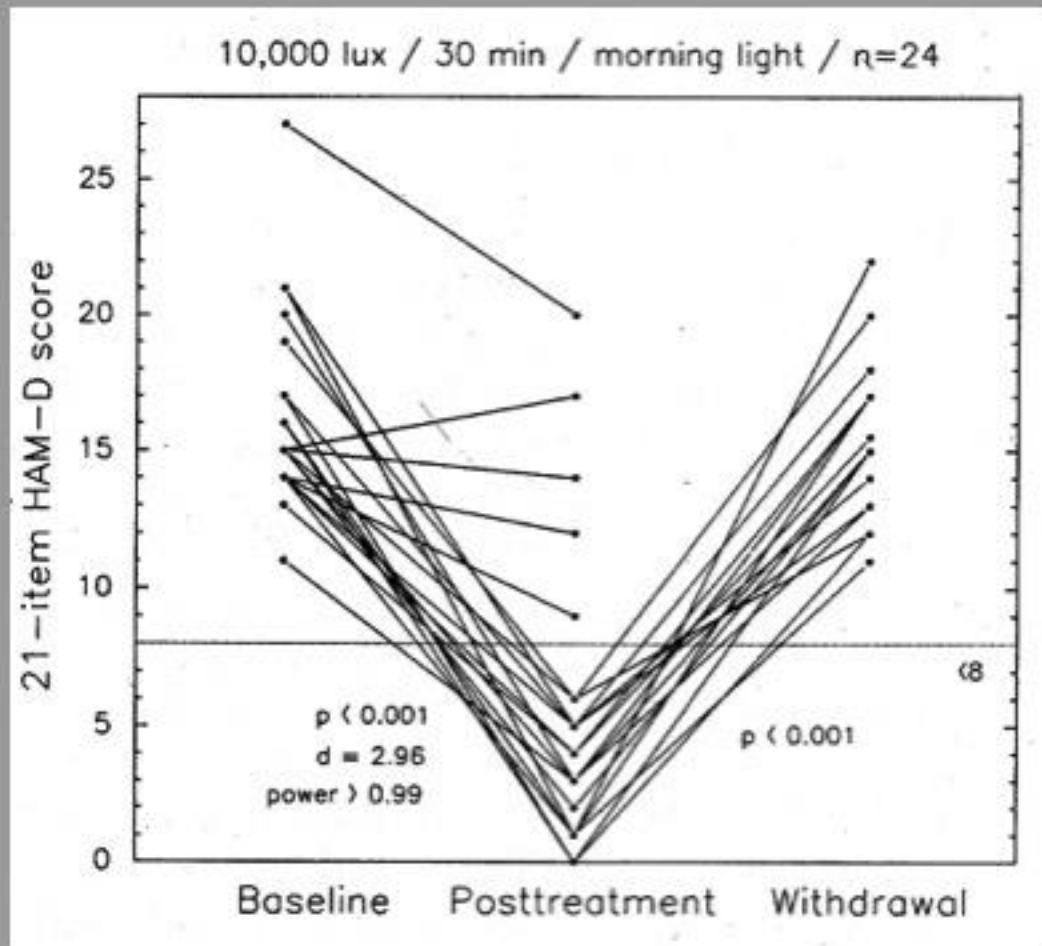
\*by the Board of Directors, Center for Environmental Therapeutics, [www.cet.org](http://www.cet.org)

# Where are the seasonal patients?



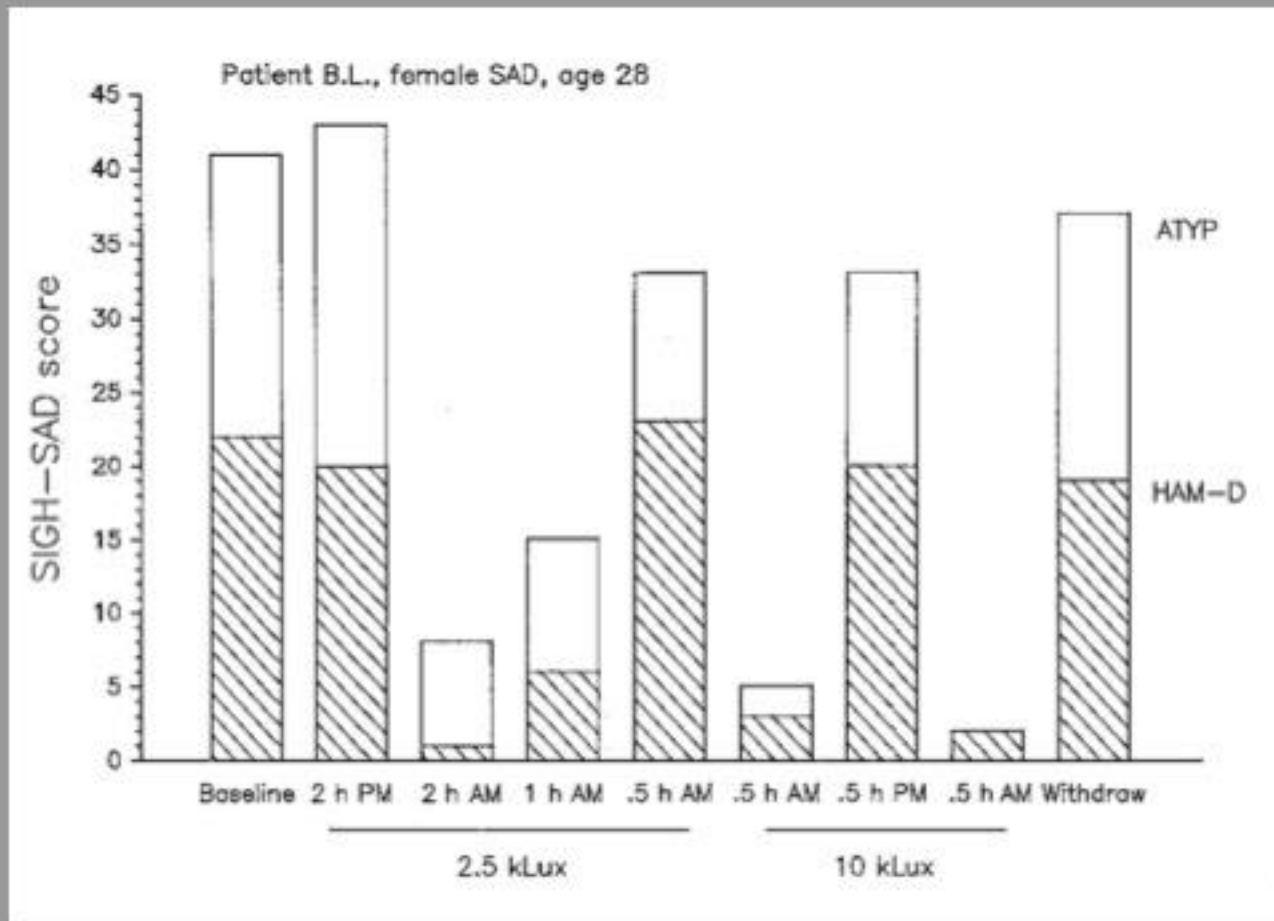
Terman M, White T (2007) Web survey for the Center for Environmental Therapeutics

## Responders and nonresponders to bright light therapy



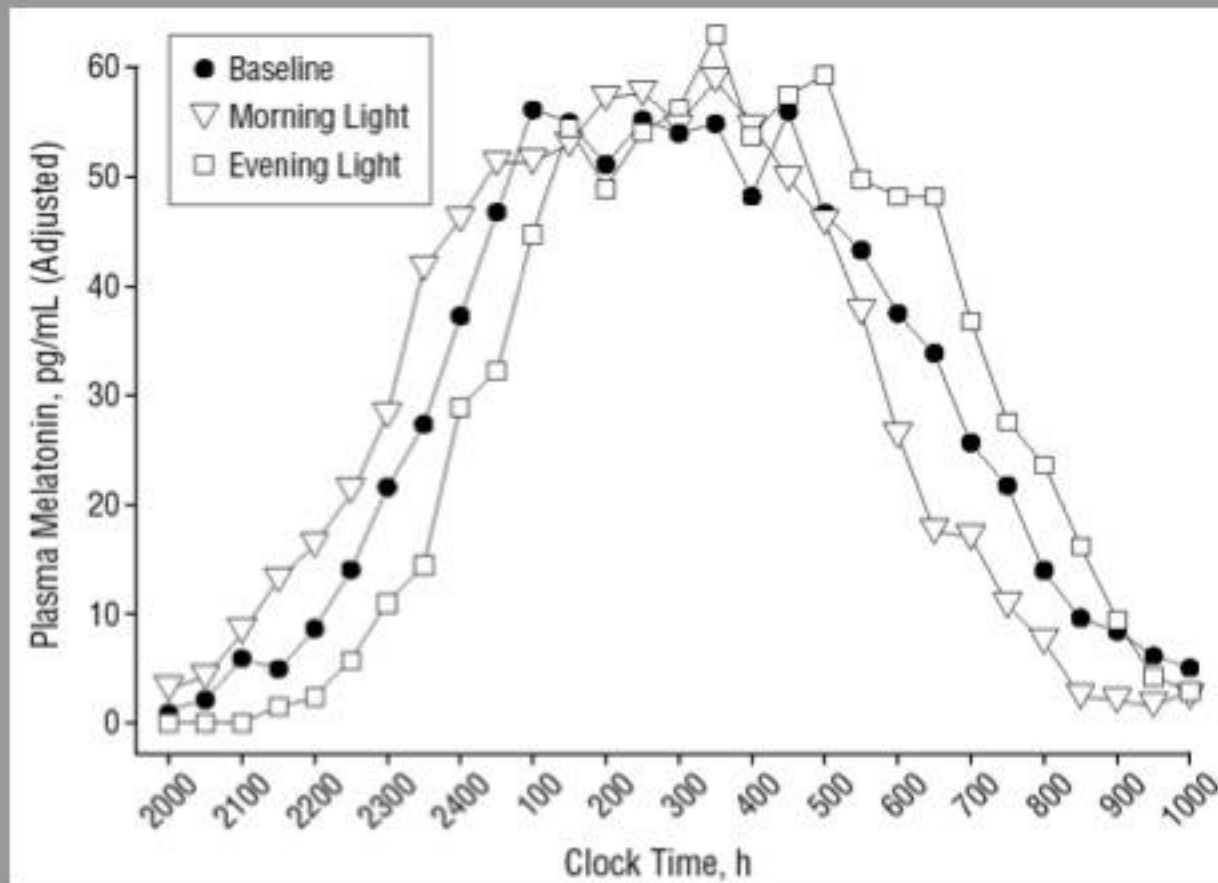
Terman JS, Terman M, Schlager D, Raftery B, Rosofsky M, Link MJ, Gallin PF, Quitkin FM (1990) Efficacy of brief, intense light exposure for treatment of winter depression. *Psychopharmacology Bulletin* 26: 3-11.

## Dose-response for antidepressant light therapy: Intensity, duration, time of day



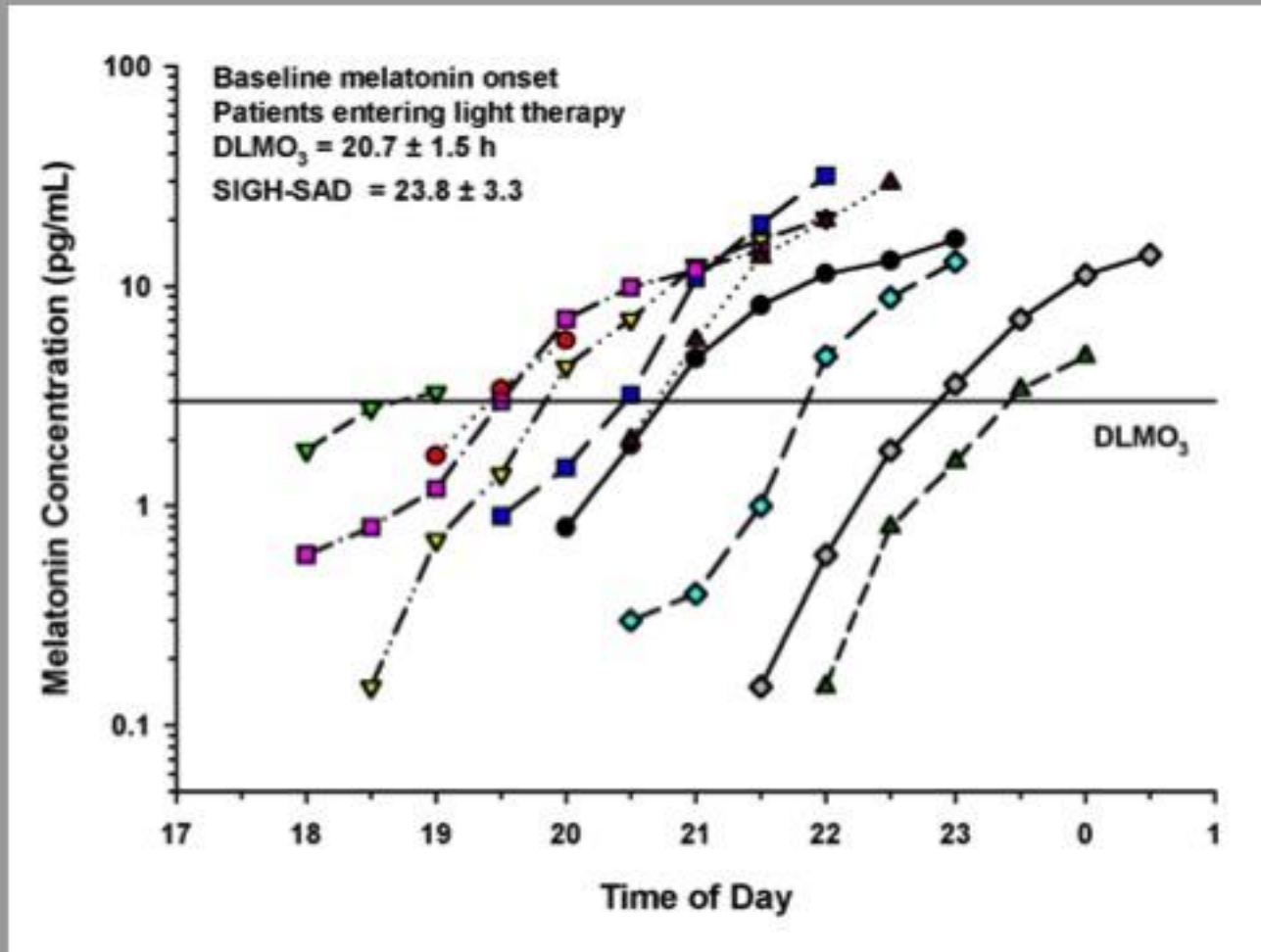
Terman M. (1988) On the question of mechanism in phototherapy for seasonal affective disorder: Considerations of clinical efficacy and epidemiology. *Journal of Biological Rhythms* 3:155-172

# Response of the melatonin rhythm to morning or evening light exposure



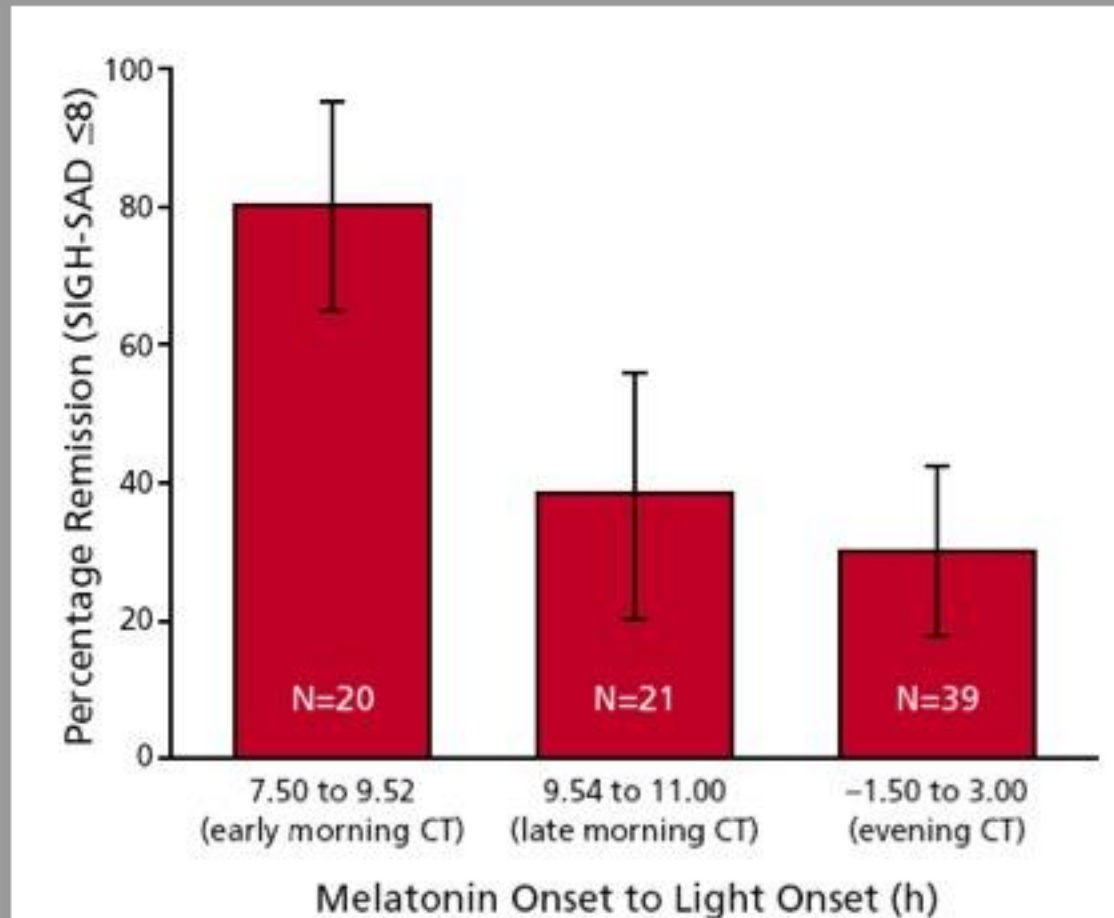
Terman JS, Terman M, Lo ES, Cooper TB. (2001) Circadian time of morning light administration and therapeutic response in winter depression. *Archives of General Psychiatry* 58:69-75

# Individual differences in circadian timing



$DLMO_3$  = dim light melatonin onset defined as salivary concentration  $\geq 3$  pg/mL

The antidepressant effect of light therapy depends on the timing of exposure relative to baseline circadian phase while depressed.





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## Automated Online Confidential Self-Assessments

A service of CET offered anonymously and free of charge.

Complete our three unique questionnaires to help you clarify:



### Your diagnostic status (AutoPIDS)

Bright light therapy has been established as the international standard for treatment of winter depression, milder "winter doldrums," and other chronobiological, circadian rhythm sleep and mood disturbances.



### Your circadian rhythm type (AutoMEQ)

How much of a lark or owl are you, compared with other people? When does your internal clock think you should be going to sleep? If you are taking light therapy, what would be the most effective time of day?



### Your current level of depression (AutoSIGH)

Whether or not you're under treatment for depression, it is important to track changes in your state toward improvement (or not). You should know your score and details about your symptom pattern, which can facilitate discussions with your doctor.



## AutoMEQ

### Automated Morningness-Eveningness Questionnaire (AutoMEQ)

0%  100%

Approximately what time would you get up if you were entirely free to plan your day?

Please choose...

- 1) 5:00–6:30 a.m.
- 2) 6:30–7:45 a.m.
- 3) 7:45–9:45 a.m.
- 4) 9:45–11:00 a.m.
- 5) 11:00 a.m.–12:00 noon
- 6) 12:00 noon–5:00 a.m.



(You may want to use your browser's zoom function to maximize the size of the question text on your screen.)

Resume later

<< Previous

Next >>

Exit and clear survey

0%  100%

How hungry do you feel during the first half hour after you wake up?

Please choose...

- 1) Not at all hungry
- 2) Slightly hungry
- 3) Fairly hungry
- 4) Very hungry

Resume later

<< Previous

Next >>

Exit and clear survey

# immediate, personalized feedback...



AutoMEQ

Automated Morningness-Eveningness Questionnaire (AutoMEQ)

0% ☐ 100%

## HERE IS YOUR PERSONALIZED AUTO-MEQ FEEDBACK

Your score is **52**.

**YOUR MORNINGNESS-EVENINGNESS TYPE IS CONSIDERED TO BE INTERMEDIATE.**

Morningness-eveningness scores range from 16-86. Scores of 41 and below indicate "evening types." Scores of 59 and above indicate "morning types." Scores between 42-58 indicate "intermediate types."

16-30	31-41	42-58	59-69	70-86
definite evening	moderate evening	intermediate	moderate morning	definite morning

Your score allows us to estimate when your brain begins to produce the nighttime hormone melatonin\*, which normally occurs before you are ready to fall asleep.

**WE ESTIMATE THAT YOUR MELATONIN ONSET OCCURS AT ABOUT 9:45 pm.**

\*saliva concentration of 3 picograms per milliliter

The time you are first able to fall asleep easily (assuming that you keep a regular sleep schedule) is related to the time that your brain begins to produce melatonin in the evening or at night.

**WE ESTIMATE THAT YOUR "NATURAL" BEDTIME IS AT ABOUT 11:45 pm.**

This information can be put to important use if you are trying to organize your daily schedule to best match with your circadian rhythm type. It is especially useful if you want to use **light therapy** to shift your rhythms in a desired direction (morning light shifts rhythms earlier; evening light shifts them later).

Appropriate timing of therapy can help you wake up more alert for a normal work day, reduce insomnia when you are trying to get to sleep, accommodate to shift work, prepare for (or recover from) long distance air travel, and even correct abnormal sleep patterns such as the Delayed Sleep Phase Syndrome. Below, we specify two well-tested applications:

Light therapy is the first-line treatment for **Seasonal Affective Disorder**, eliminating or reducing the need to take drugs. People suffering with major depressive episodes in winter should seek supervision of treatment by a health professional knowledgeable about managing the symptoms. The personalized advice we give you here is based on a large clinical trial at Columbia Presbyterian Medical Center. That clinical trial used a **10,000 lux fluorescent light box with an overhead diffusing screen, for 30 minutes daily**. (Other light box types might require longer exposure duration, or might be less effective. You should ask your doctor to help you make adjustments to maximize the antidepressant effect.)

If you are considering 10,000 lux light therapy to combat winter depression, your morningness-eveningness score indicates that **YOUR OPTIMUM 30-MINUTE LIGHT TREATMENT SHOULD BEGIN AT 6:30 am.**

You can try the same light timing, **6:30 am**, to combat oversleeping and ease of rising in morning, whether or not you have winter depression.

Our recommendation provides only a general guideline. You may need to adjust the timing based on your experience during treatment. If you sleep longer than 7 hours per night, this schedule will require you to wake up earlier than usual for greatest benefit. Some people compensate by going to bed earlier, while others feel fine with shorter sleep.

Click **next** to print out your answers to each question, send us feedback, and go to the website for the Center for Environmental Therapeutics.

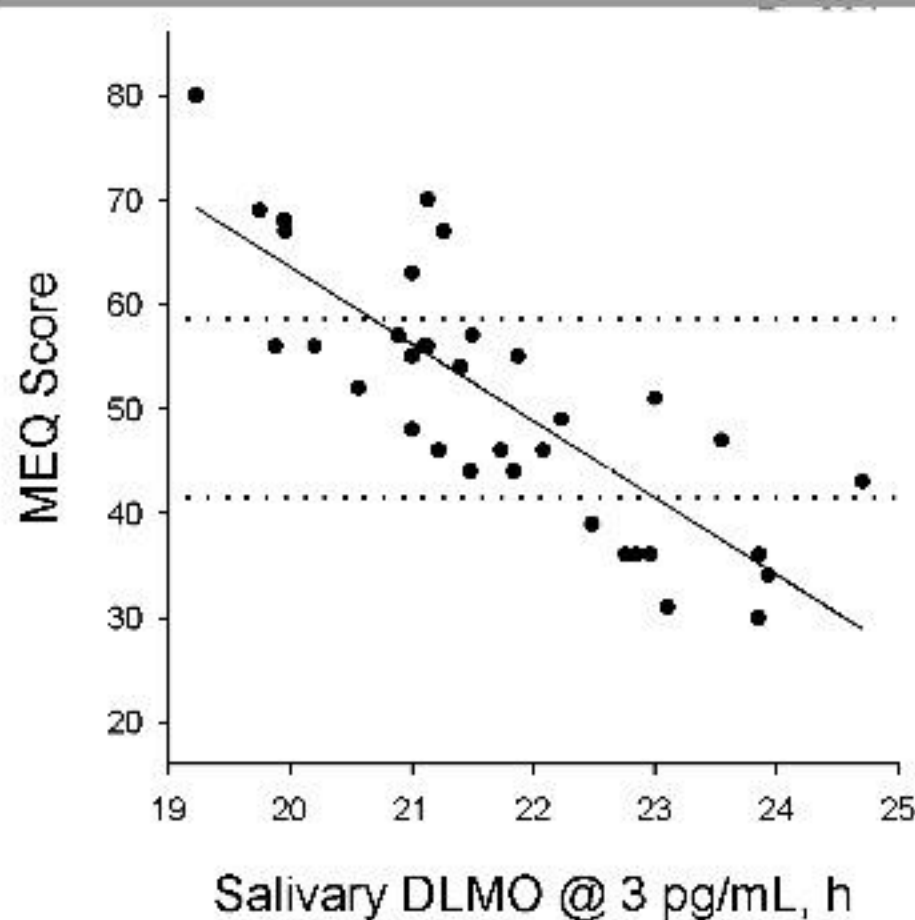
[Resume later](#)

[<< Previous](#)

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# The Horne-Östberg Morningness-Eveningness score corresponds to melatonin onset phase.



$r = -0.81$   
 $N = 35$   
 $P < .001$

morning types

intermediate types

evening types

DLMO: evening melatonin onset measured under dim light conditions

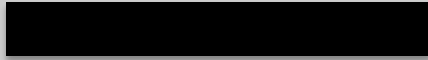
3.0 pg/mL: a low melatonin concentration chosen to index secretory onset

MEQ Score	Start Light
16-18	8:45
19-22	8:30
23-26	8:15
27-30	8:00
31-34	7:45
35-38	7:30
39-41	7:15
42-45	7:00
46-49	6:45
50-53	6:30
54-57	6:15
58-61	6:00
62-65	5:45
66-68	5:30
69-72	5:15
73-76	5:00
77-80	4:45
81-84	4:30
85-86	4:15

Lark

9 PM

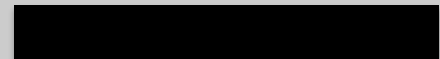
5 AM



Owl

1 AM

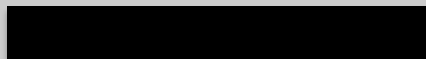
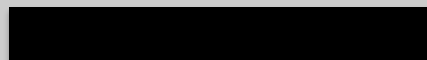
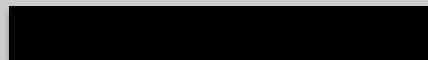
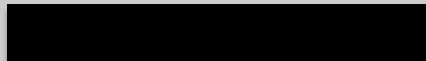
9 AM



Delayed Sleep Phase Disorder

4 AM

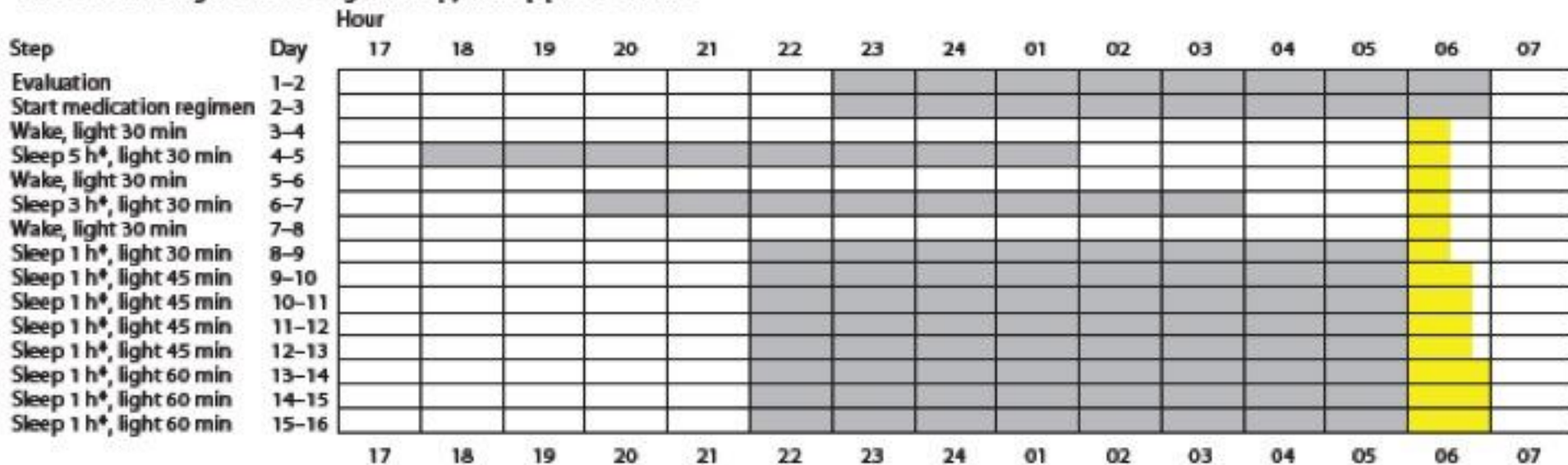
12 PM



# TRIPLE CHRONOTHERAPY

Sleep allowed, normal room light if awake; example anchored to 23–07 h habitual sleep pattern while depressed  
 Light therapy (10,000 lx, duration increased at 4 to 5-day intervals if tolerated and improvement is slow)

## Three alternate nights awake + light therapy + sleep phase advance



**Fig. 25.** Under the complete chronotherapeutics protocol, phase advanced sleep alternates with full nights awake but moves back in 2-hour steps toward a maintenance sleep phase one hour earlier than at baseline. \* Advanced.

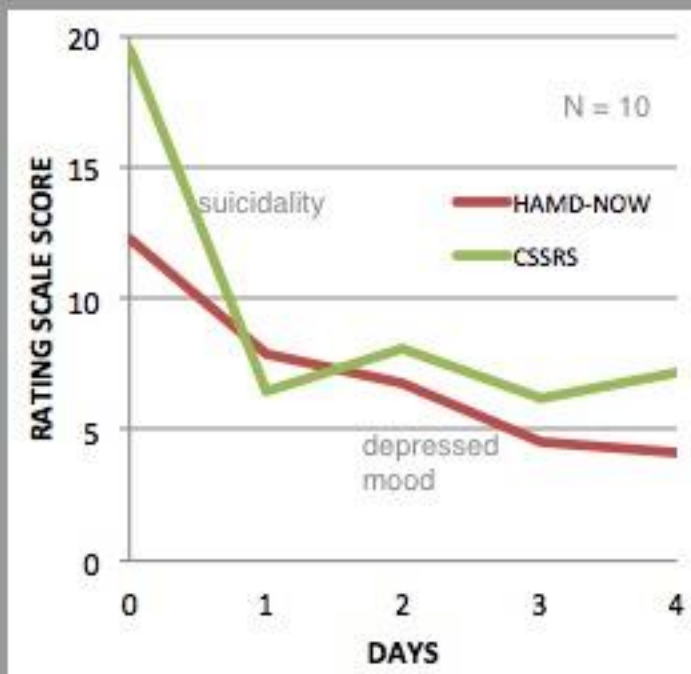
Wirz-Justice A, Benedetti F, Terman M (2013) *Chronotherapeutics for Affective Disorders: A Clinician's Manual for Light and Wake Therapy*. 2nd edition, revised. Basel, Karger.

# Triple Chronotherapy

## The South Carolina Study

Day	1p	2p	3p	4p	5p	6p	7p	8p	9p	10p	11p	12a	1a	2a	3a	4a	5a	6a	7a	8a	9a	10a	11a	12p
Pre																								
0																							X	
1																							X	
2																							X	
3																							X	
4																							X	
Post																								

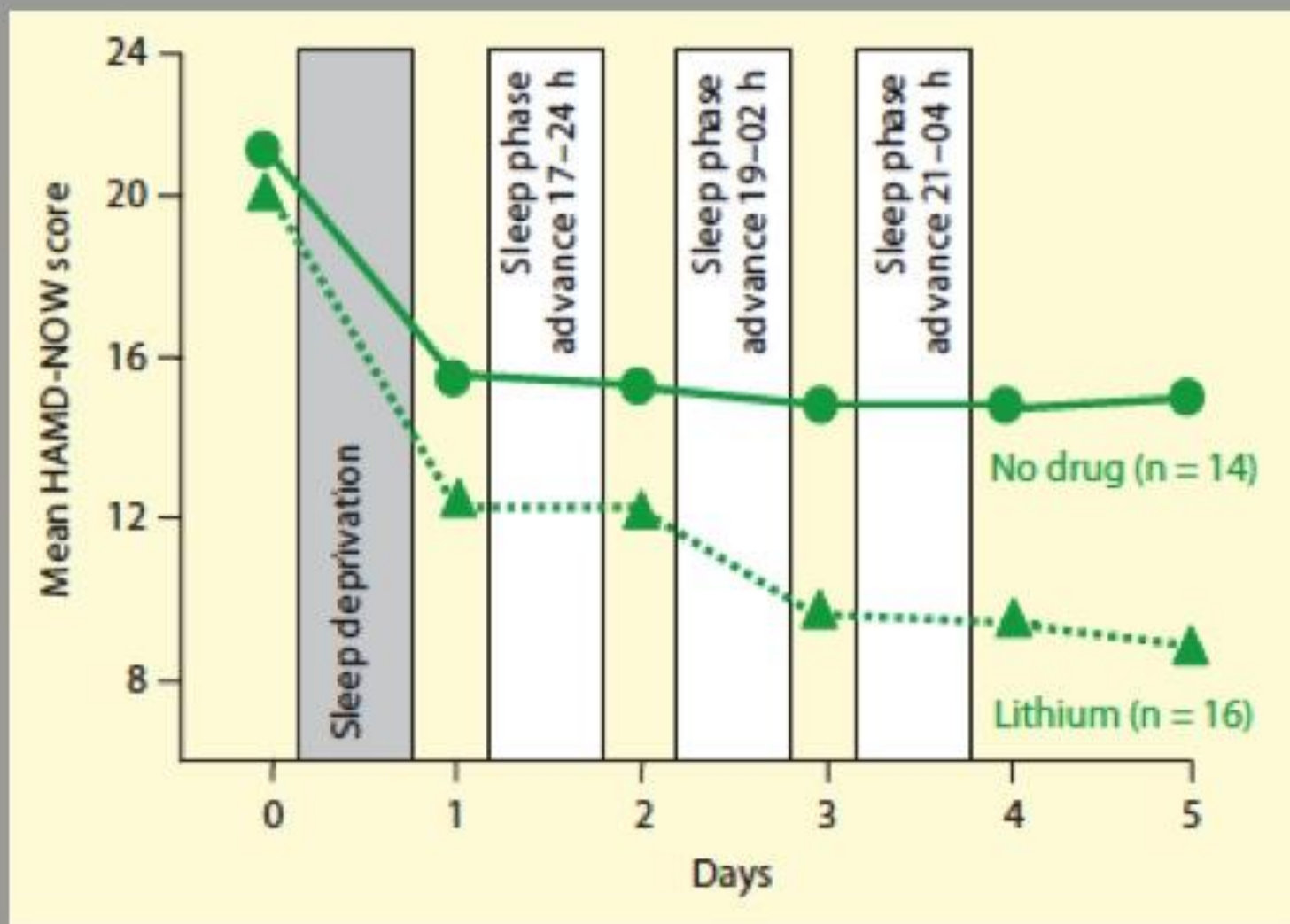
Wake	Sleep	Light	Assessment
			X



Gregory Sahlem & colleagues  
Department of Psychiatry  
Medical School of South Carolina

In press, 2014  
Journal of Psychiatric Research

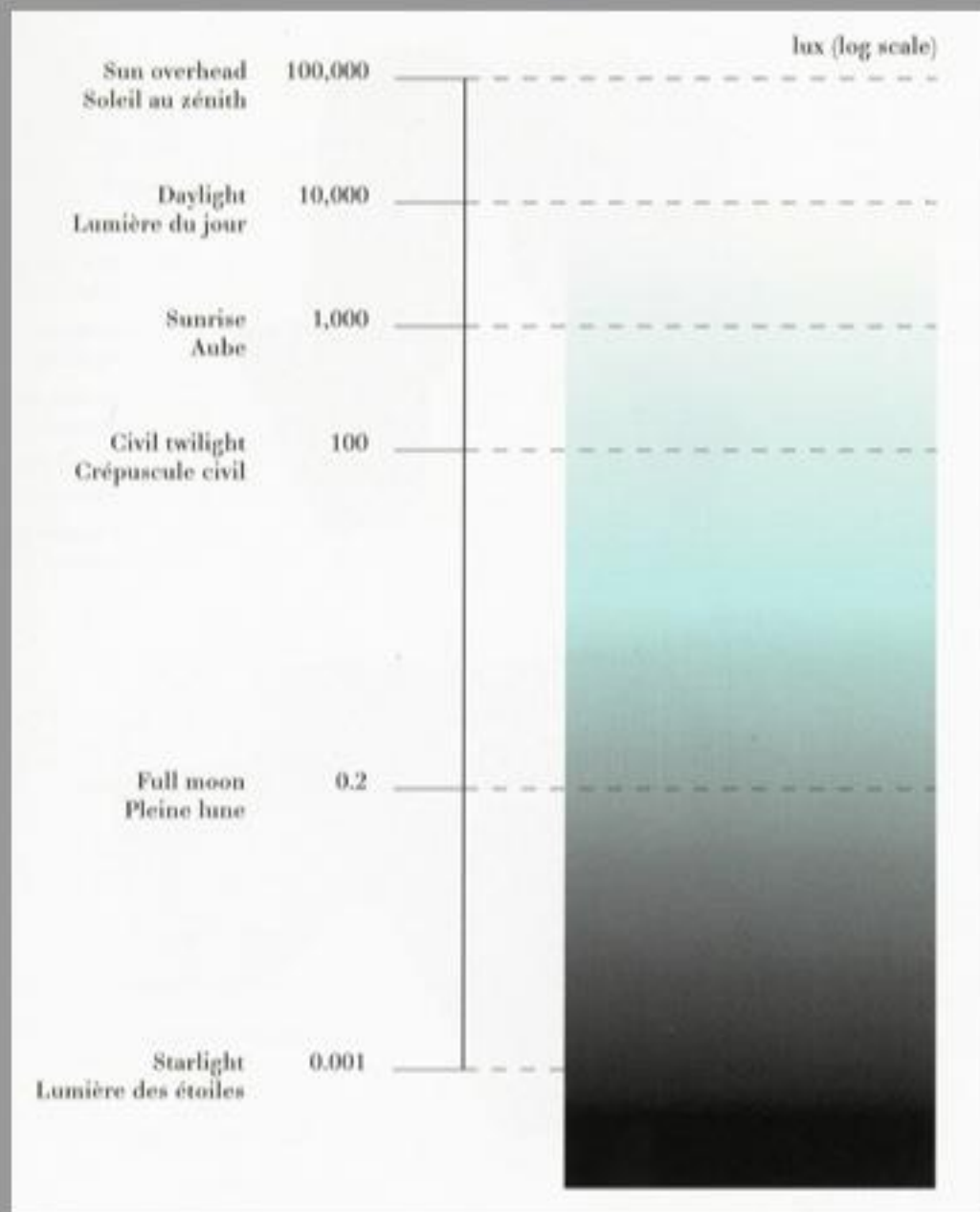
# Triple chronotherapy + lithium for bipolar I disorder



Benedetti F, Barbini B, Campori E, Fulgosi MC, Pontiggia A, Colombo C (2001) Sleep phase advance and lithium to sustain the antidepressant effect of total sleep deprivation in bipolar depression: new findings supporting the internal coincidence model? *Journal of Psychiatric Research* 35:323–329.



# Dawn and Dusk Simulation



BIOMEDICAL

SUMMER 1999  
VOL. 2, ISSUE 3

# FRONTIERS

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COLUMBIA-PRESBYTERIAN MEDICAL CENTER

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Relief for TMJ

## A SUNRISE/SUNSET SIMULATING MACHINE TREATS DEPRESSION

An electronic device that mimics the dawn's early light of spring or summer can help people who suffer from clinical depression in the winter and fall due to their seasons' shorter daylight hours, say the Columbia University researchers.

"Seasonal daylight hours in the fall and winter can make many people in the middle- and north latitudes very mood dependent," says Dr. Michael Terman, associate professor of clinical psychology and director of the Clinical Chronobiology Program at the New York State Psychiatric Institute. "But when spring and summer come, their good mood returns and they become energetic."

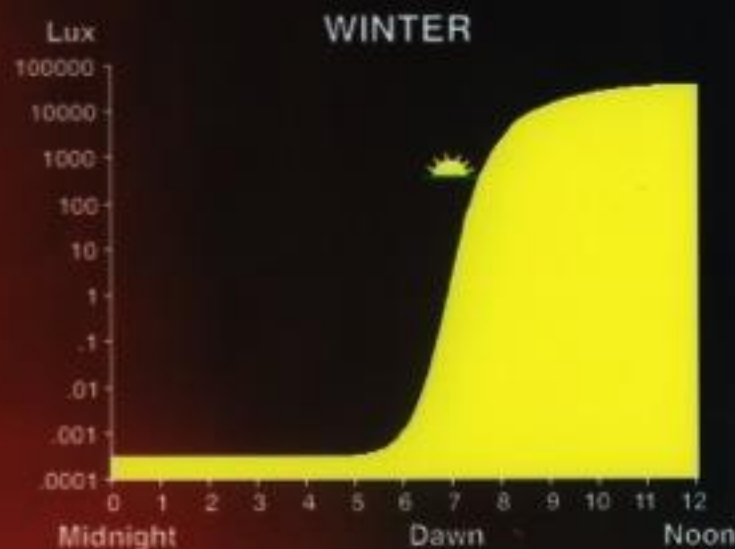
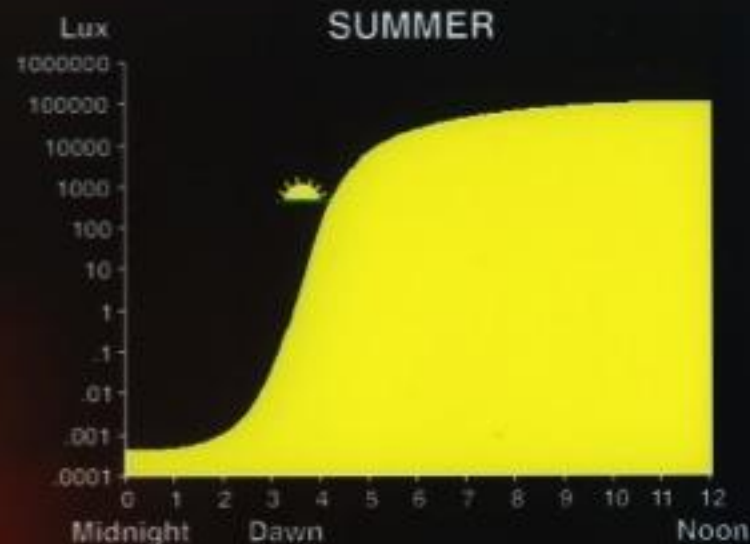
He and colleagues thought that if they could imitate the lighting pattern of the spring season, they could possibly treat

(Continued on page 6)

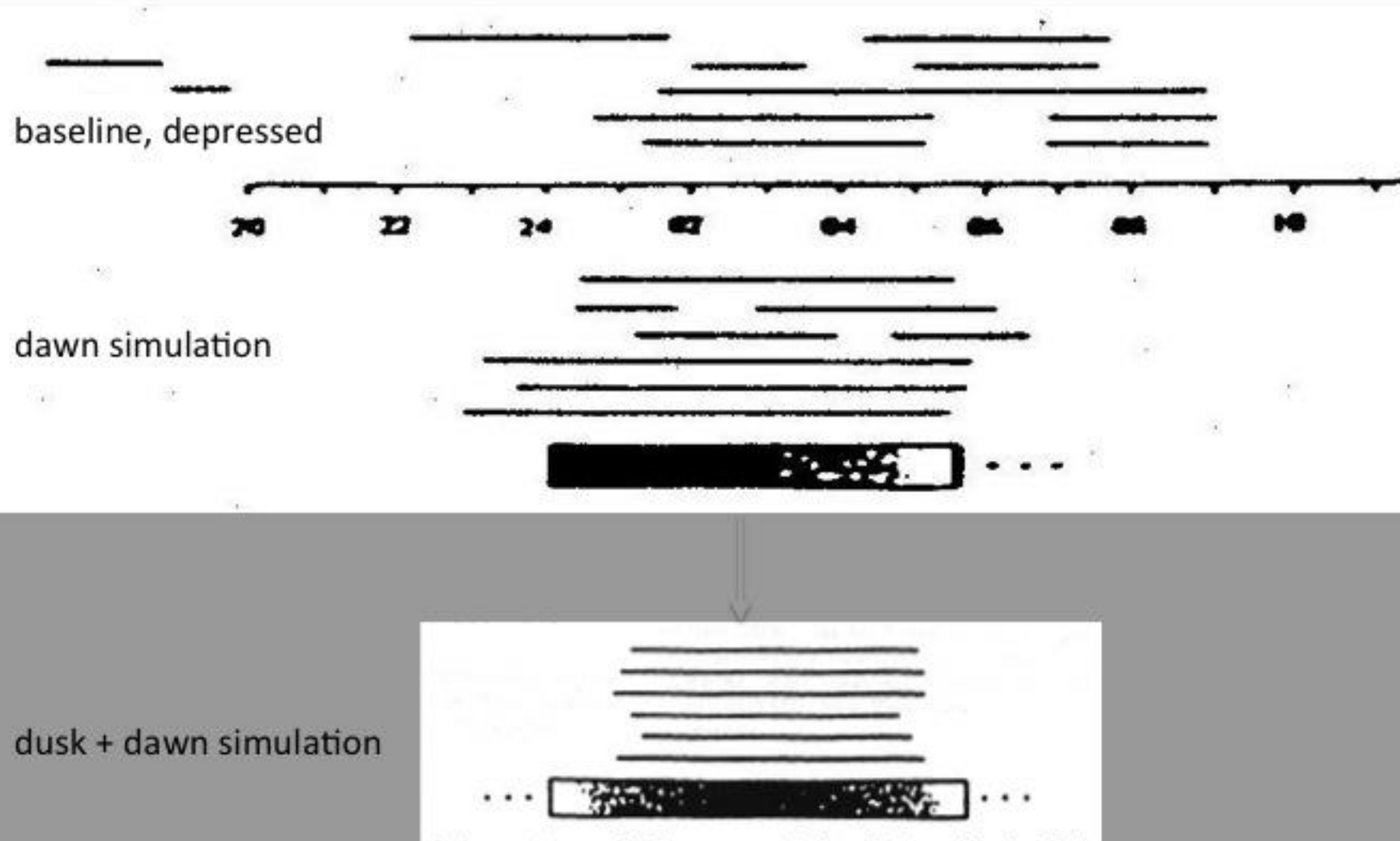
Special Report  
Medical Devices at  
Columbia

A sleeping person bathes in the simulated light of a summer's dawn.

Photo by Greg Gorman, Science/AA

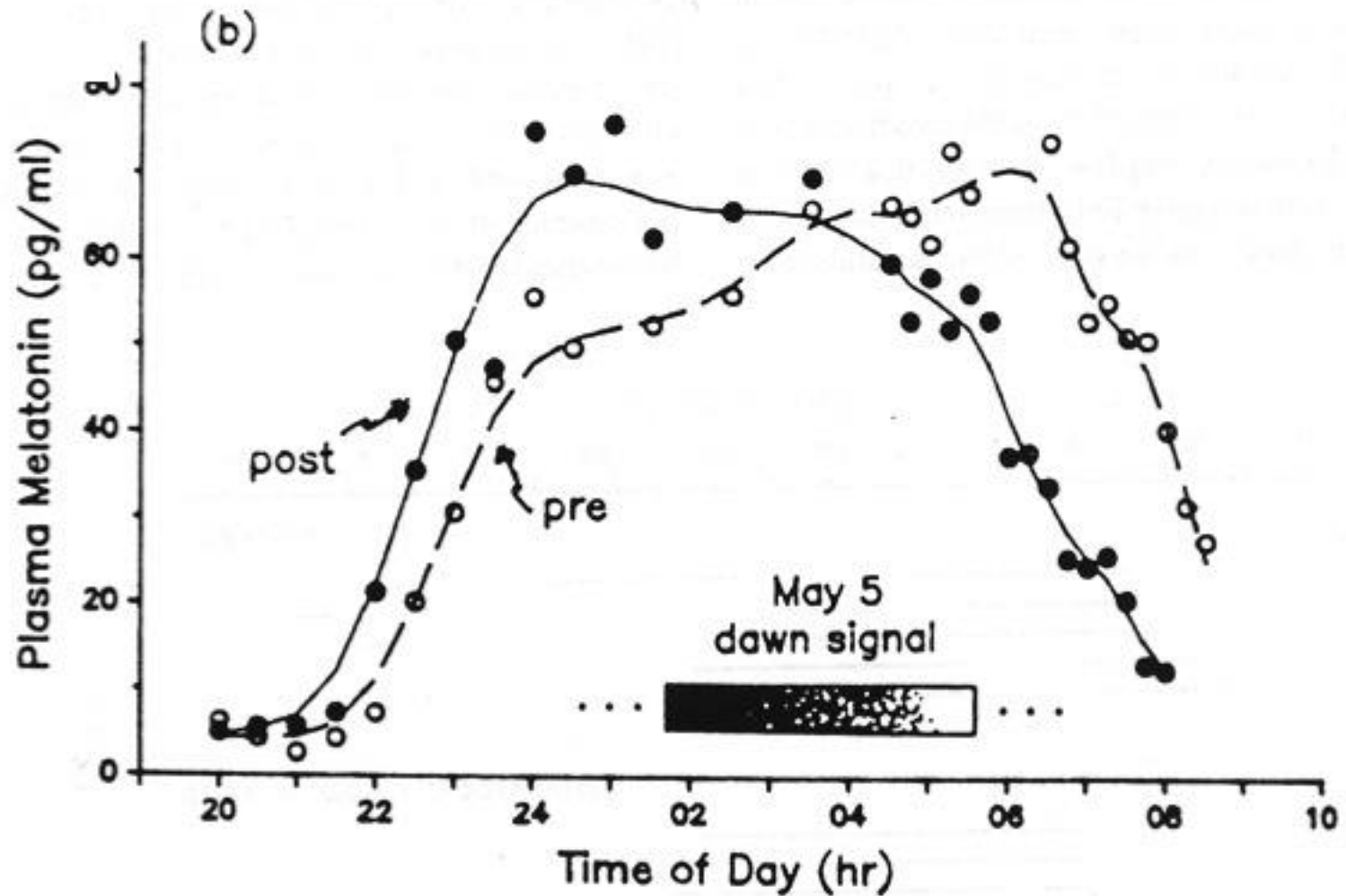


# Normalization of sleep accompanies antidepressant response to twilight simulation



Terman M, Schlager D. Twilight therapeutics, winter depression, and sleep. In Montplaisir J, Godbout R, Eds. *Sleep and Biological Rhythms*. New York: Oxford University Press 1990;113-128.

## Gradual Bedroom Dawn Illumination Phase Advances the Melatonin Cycle



Terman M, Schlager D et al. (1989) Dawn and dusk simulation as a therapeutic intervention. *Biological Psychiatry* 25:966-970.



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## Products and Select Solutions

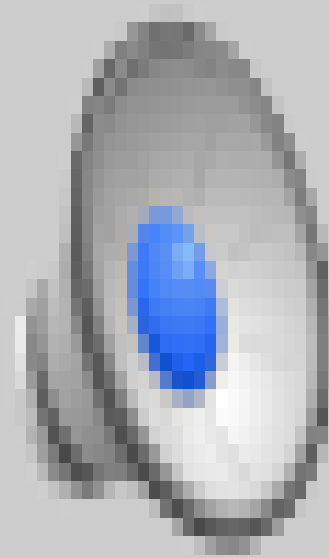


### Smart Lamp

International research has shown that dawn simulation is capable of re-setting circadian body rhythms to help you wake up the way nature intended. Dawn simulation therapy is spearheaded by Dr. Avery (University of Washington) and CET President Dr. Terman (Columbia University).

Recommended lamp positions for dawn and dusk simulation:





Dusk-to-dawn simulator for hospitals and elder-care homes

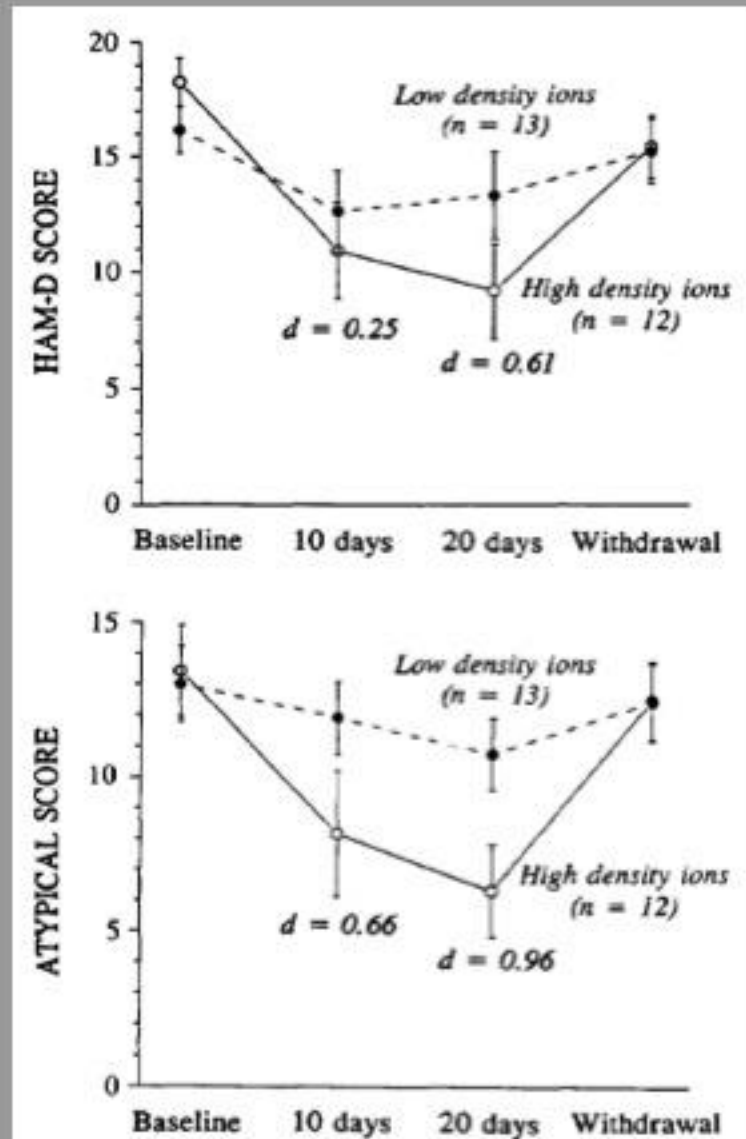
# Negative air ionization



## High-output negative air ionizer with grounded wrist strap



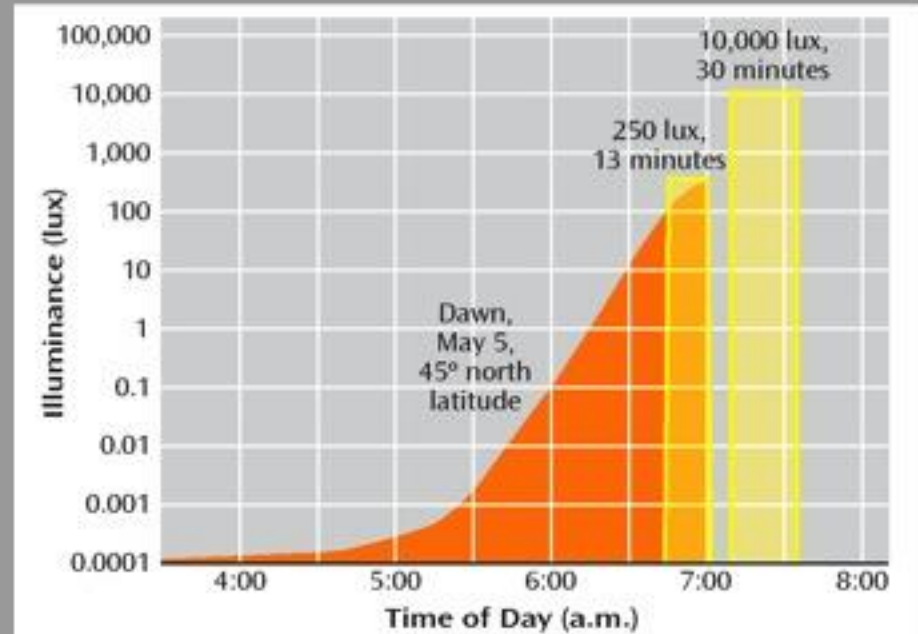
## The first controlled trial of negative air ionization for 30 min upon wake-up



Terman M, Terman JS. (1995) Treatment of seasonal affective disorder with a high-output negative ionizer. *Journal of Alternative and Complementary Medicine* 1:87-92.

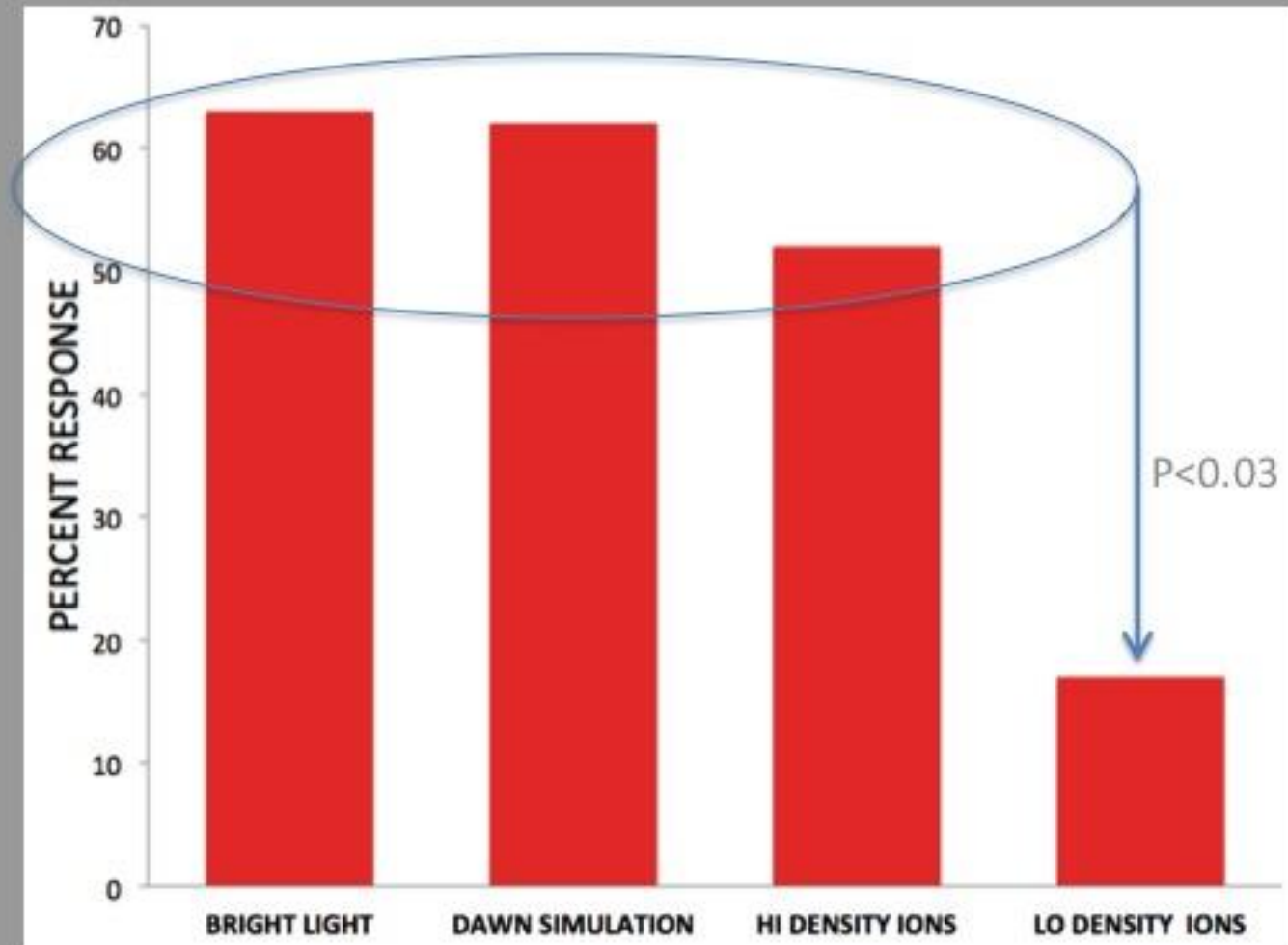
# Comprehensive head-to-head clinical trial

- Bright light therapy
- Dawn simulation therapy
- Negative ion therapy
- Placebo



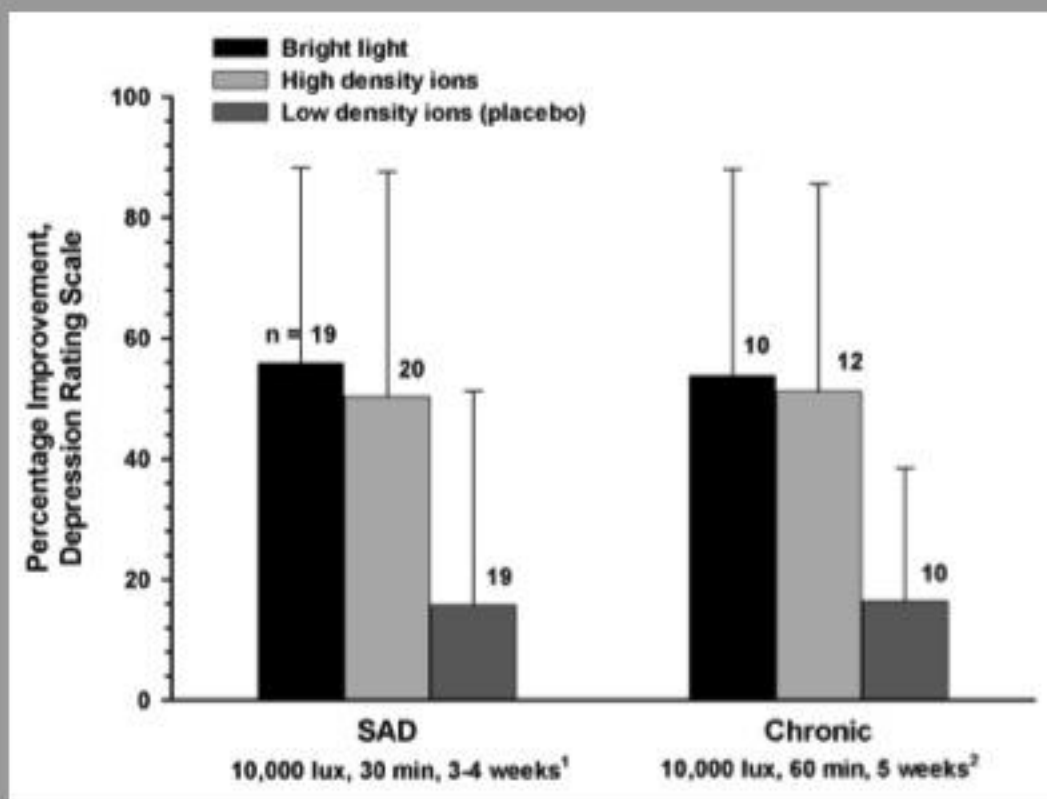
Terman M, Terman JS (2006) Controlled trial of naturalistic dawn simulation and negative air ionization for seasonal affective disorder. *Am J Psychiatry*, 163:2126-2133.

# Active vs. placebo in head-to-head trial



Terman M, Terman JS (2006) Controlled trial of naturalistic dawn simulation and negative air ionization for seasonal affective disorder. *American Journal of Psychiatry* 163:2126-2133.

Response to light therapy and negative air ionization is similar in seasonal and nonseasonal depression.



SAD: Terman et al., *American Journal of Psychiatry* 2006

Chronic: Goel et al., *Psychological Medicine* 2005

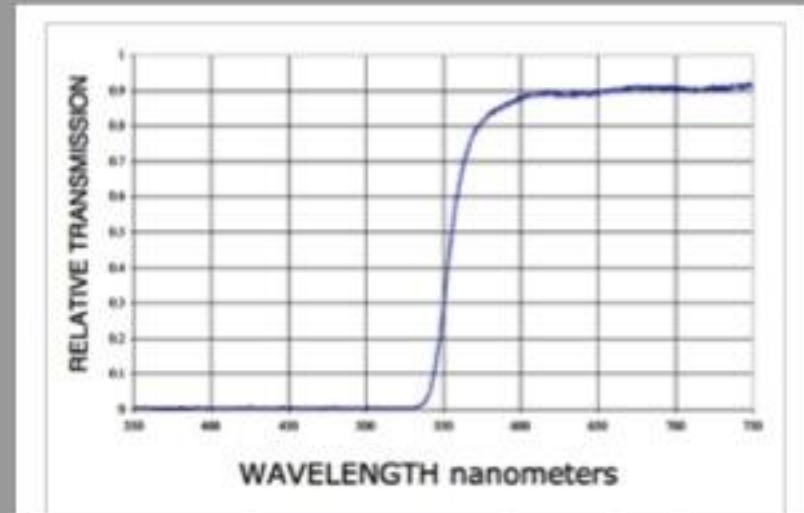
# Whole-Room Air Ionization



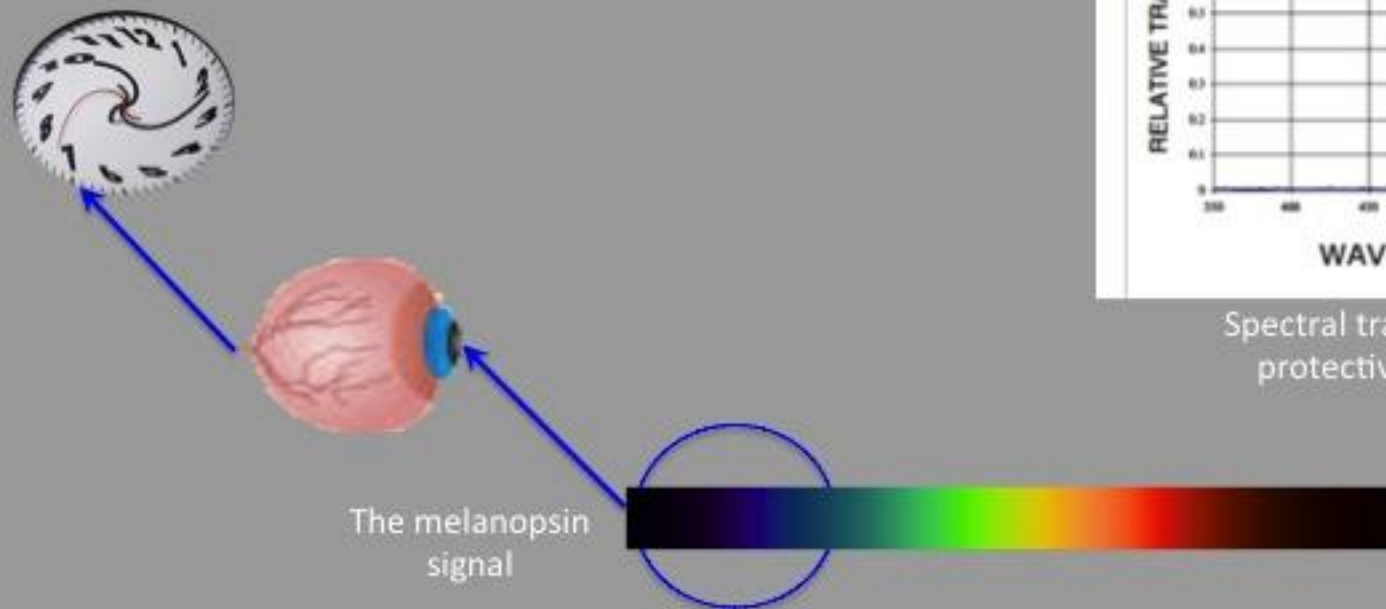
# Dark Therapy and Melatonin

# Circadian darkness vs. absolute darkness

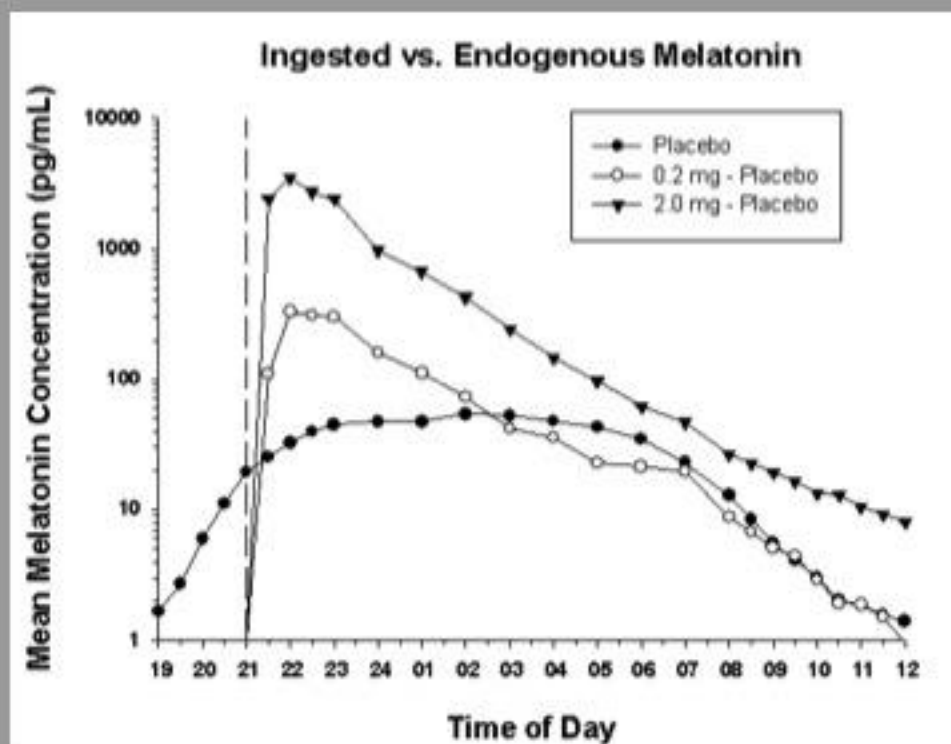
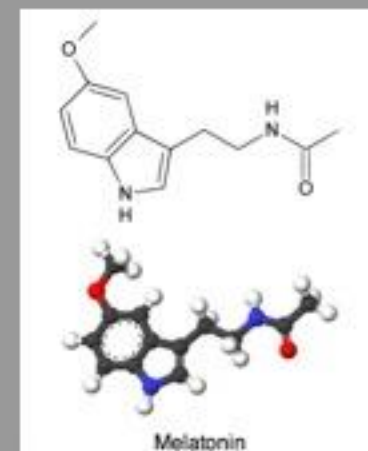
We can protect the inner clock from spurious phase shifts while maintaining clear visibility



Spectral transmission of specialized protective lenses, [www.cet.org](http://www.cet.org)



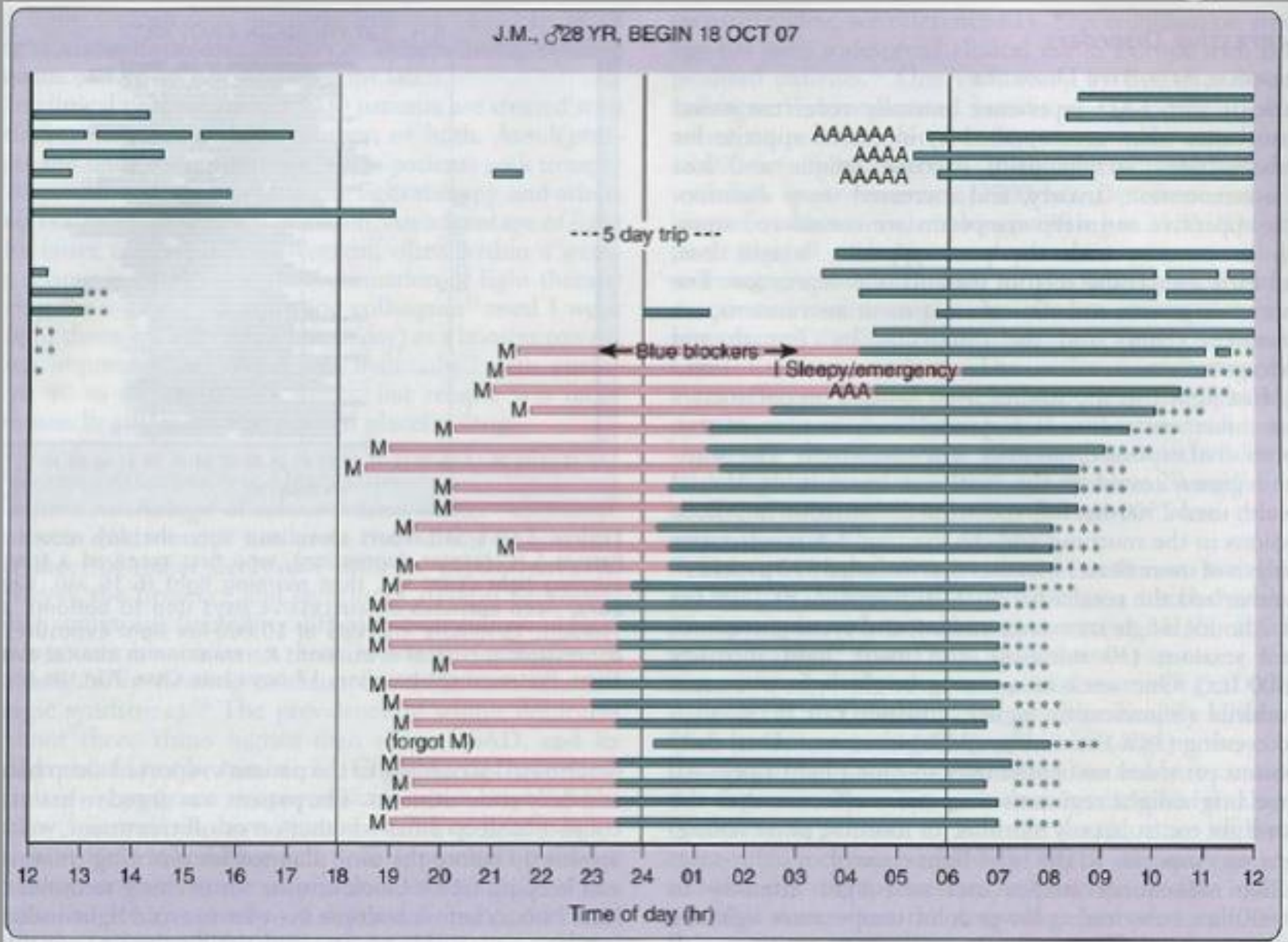
Melatonin itself is a chronobiotic that works in antiphase with light.



"Microdose Melatonin"  
0.2 mg sustained release  
Product pending, 2015  
Center for Environmental Therapeutics  
For notification: [melatonin@cet.org](mailto:melatonin@cet.org)

Terman M. Final Report to the Sleep Research  
Society Foundation, Eliot D. Weitzman Prize, 2007

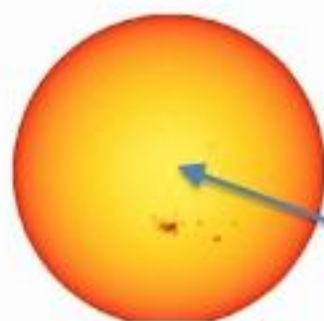
## Combination treatment: melatonin + light



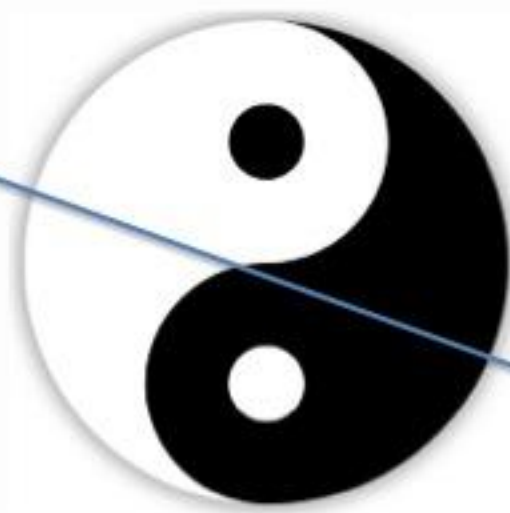
Terman M, Terman JS. (2010) Light therapy. In *Principles and Practice of Sleep Medicine* (5th ed.), Kryger MH, Roth T, Dement WC, Eds. St. Louis, Elsevier/Saunders, pp. 1682-1695.

*(To me, this sounds like Western physics...)*

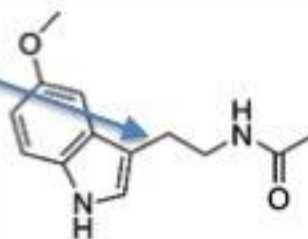
Wikipedia: In Chinese philosophy, **yin and yang**, which are often shortened to "yin-yang" or "yin yang", are concepts used to describe how apparently opposite or contrary forces are actually **complementary, interconnected and interdependent** in the natural world, and how they give rise to each other as they interrelate to one another.



NASA



I CHING



AARON LERNER

# Resources for yourself and your patients



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[sltbr.org](http://sltbr.org)

UNC Library,  
Chapel Hill

## Chronotherapy

Take control of your inner clock

by Ian McMahan, Ph.D., and Michael Terman, Ph.D.

### Sleep and Memory As We Age: The Brain Puzzle



Everyone thinks about the poor sleep and memory lapses common in old age, and our anxiety is magnified by the mystery of what's going on. New data point to specific brain changes that are normal to old age. Might chronotherapy help?

[Read More](#)

### Light Therapy, Antidepressant Meds—Either/Or? Both?



Light therapy can fight both seasonal and nonseasonal depression. Nonseasonal includes bipolar and major depressive disorders, and depression during pregnancy and old age. Then there is depression that worsens in winter but is not "on-and-off" like SAD. Where do drugs fit in? [Read More](#)

### Light Therapy on the Wild Side



In the quest for novelty and consumer interest, some companies have turned away from bright white light boxes (the clinically-tested standard). Ill-advised variations include miniaturization and head or eyeglass mounts. Green and blue have been substituted for white on the doubtful supposition that the antidepressant effect would be enhanced. [Read More](#)

### Light Therapy Good, Bunkum Bad



It's not just a matter of switching on bright lights. So many factors are at play. We rely on clinical trials to show what works and what doesn't. Fortunately, we know a lot. Unfortunately, too many light therapy devices have not seen adequate testing. [Read More](#)

For clinicians and hospital  
administrators

For patients, general readers,  
and clinicians new to principles  
of circadian timing

Anna Wirz-Justice  
Francesco Benedetti  
Michael Terman

2nd, revised edition

## Chronotherapeutics for Affective Disorders

A Clinician's Manual for Light and Wake Therapy



- paperback
- e-book

KARGER

both  
published  
in 2013

"Breakthrough therapy for insomnia, depression, and circadian rhythm regulation!"

—Robert Arnot, M.D., author of  
Dr. Bob Arnot's Guide to Turning Back the Clock

## Reset Your Inner Clock

The Drug-Free Way to Your  
Best-Ever Sleep, Mood, and Energy

Michael Terman, PhD

Director, Center for Light Treatment and Biological Rhythms  
Columbia University Medical Center

Ian McMahan, PhD

City University of New York



Previously published as *Chronotherapy*

- paperback
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- Audible

# Society for Light Treatment and Biological Rhythms

[www.sltbr.org](http://www.sltbr.org)



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The Society of Light Treatment and Biological Rhythms (SLTBR) is an international scientific non-profit organization devoted to promoting research and knowledge about the effects of light on the organism and the chronobiology of psychiatric as well as other medical disorders.

Founded in 1988, the SLTBR has brought together leading scientific experts, clinicians, and interested participants from different professional and multi-disciplinary backgrounds for discussion and exchange on the science and practical application of chronotherapy in medicine.

Join us for our 27<sup>th</sup> Annual Meeting, June 2015, San Diego  
[info@sltbr.org](mailto:info@sltbr.org)

CET is for patients, prospective patients, their families, students, and general-interest readers.



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## Ask the Doctor

**Q:** I notice an antidepressant effect if I use my light box in the early morning. However, I am phase-advanced, so I do not sleep well if I use the light in the morning. However, when I use the light in the evening, I do not notice an antidepressant effect. Would I get the effect by using the light in the mid-morning plus the evening?

There is no harm trying, but we cannot confidently predict the result. It has been hypothesized that "early types" need a phase delay (from evening light) to show the antidepressant effect, while "late types" will respond to phase advances (from morning light). Thus far, there are no strong data to support for that hypothesis — most people respond to phase advances, regardless of their chronotype. [Read More](#)

## Self-assessment



Take a free, confidential survey with personal feedback to share with your doctor or therapist.

When does your internal clock think you should be go to sleep? If you are using light therapy, what would be the most effective time of day for you? How can you track your symptoms, if you are depressed?

*We write simply, but with care for accuracy*

# CET is for clinicians, support staff, and administration



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## The Chronotherapeutics Forum

Join in discussion, debate, brainstorming and mutual support for doctors, mental health professionals, and chronobiologists.

Members share experiences, and solve puzzles together.

This forum is restricted to doctors, psychiatrists, psychologists, other mental health professionals, and chronobiologists with a clinical bent.

The forum is privacy-protected: Posts are not for distribution and cannot be googled.

Because the forum is designed to stimulate interaction among the caretaker peer group, those without direct clinical responsibility (e.g., industrial or university R&D, manufacturing or marketing) are not included.

Consumers and patients have a separate forum, [Ask the Doctor](#).

[Apply to Join Here](#)

### Login To the Forum

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