Chronotherapeutics: Light Therapy and Beyond

Michael Terman, Ph.D.
Disclosures

- I have no relevant financial relationship with the manufacturers of any commercial products and/or providers of commercial services discussed in this CME activity.

- Neither I nor any member of my immediate family has a financial relationship or interest with any proprietary entity producing health care goods or services related to the content of this CME activity.

- 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

Circadian rhythms in synchrony with sleep

Core body temperature

Plasma melatonin

Time of Day (h)
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
Where are the seasonal patients?

![Graph 1: Proportion of winter depression vs. latitude N.](image1)

- **Graph 1:**
  - **Equation:** $y = 0.018x - 0.336$
  - **$r^2$:** 0.998
  - **Data Points:**
    - 26-30: 0.2
    - 30-34: 0.3
    - 34-38: 0.4
    - 38-42: 0.5
    - 42-46: 0.4
    - 46-50: 0.3

![Graph 2: Proportion of winter depression vs. longitude.](image2)

- **Graph 2:**
  - **Equation:** $y = 0.007x + 0.304$
  - **$r^2$:** 0.987
  - **Data Points:**
    - 0-5: 0.3
    - 5-10: 0.4
    - 10-15: 0.5
    - 15-20: 0.6
    - 20-25: 0.7

North Carolina

Terman M, White T (2007) Web survey for the Center for Environmental Therapeutics
Responders and nonresponders to bright light therapy

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

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

Baseline melatonin onset
Patients entering light therapy
$DLMO_3 = 20.7 \pm 1.5$ h
$SIGH-SAD = 23.8 \pm 3.3$

$DLMO_3 = \text{dim light melatonin onset defined as salivary concentration} \geq 3 \text{ pg/mL}$
The antidepressant effect of light therapy depends on the timing of exposure relative to baseline circadian phase while depressed.

![Graph showing percentage remission (SIGH-SAD ≤8) with different exposure times.](Image)

**Melatonin Onset to Light Onset (h)**

- 7.50 to 9.52 (early morning CT): N=20
- 9.54 to 11.00 (late morning CT): N=21
- -1.50 to 3.00 (evening CT): N=39

Arch Gen Psychiatry 2001
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)

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.)

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
immediate, personalized feedback...

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**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.

<table>
<thead>
<tr>
<th>Score Range</th>
<th>Definite Evening</th>
<th>Moderate Evening</th>
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<th>Moderate Morning</th>
<th>Definite Morning</th>
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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 minute.

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 by a health professional knowledgeable about managing the symptoms. The personalized advice we give 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 may 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.
The Horne-Östberg Morningness-Eveningness score corresponds to melatonin onset phase.

Terman M, Terman JS (2005) Light therapy for seasonal and nonseasonal depression: efficacy, protocol, safety and side effects. CNS Spectrums, 10:647-663
Delayed Sleep Phase Disorder

Lark
9 PM - 5 AM

Owl
1 AM - 9 AM

4 AM - 12 PM
**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.*

## Triple Chronotherapy

**The South Carolina Study**

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### Wake, Sleep, Light, Assessment

- **Wake**: Highlighted in green
- **Sleep**: Highlighted in yellow
- **Light**: Highlighted in red
- **Assessment**: Blank cell

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**Graph 1**: Rating Scale Score

- **HAMD-NOW**
- **CSSRS**

**Axis**:
- X-axis: Days
- Y-axis: Rating Scale Score

**Legend**:
- **suicidality**: Red line
- **depressed mood**: Green line

- **N = 10**

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**Credit**

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

Dawn and Dusk Simulation
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 these seasons' shorter daylight hours, says the study's lead investigator and director of the ChronoTherapy 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 induce the lighting pattern of the solar clock, they could possibly treat..."
Normalization of sleep accompanies antidepressant response to twilight simulation

Gradual Bedroom Dawn Illumination Phase Advances the Melatonin Cycle

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

$O_2^- \cdot (H_2O)_n$
High-output negative air ionizer with grounded wrist strap
The first controlled trial of negative air ionization for 30 min upon wake-up

Comprehensive head-to-head clinical trial

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

Active vs. placebo in head-to-head trial

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
Melatonin itself is a chronobiotic that works in antiphase with light.
Combination treatment: melatonin + light

(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.
Resources for yourself and your patients
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

Chronotherapeutics for Affective Disorders
A Clinician's Manual for Light and Wake Therapy

Anna Wirz-Justice
Francesco Benedetti
Michael Terman

2nd, revised edition

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

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

both published in 2013

- paperback
- e-book

- paperback
- Kindle
- Audible
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 27th Annual Meeting, June 2015, San Diego
info@sltbr.org
CET is for patients, prospective patients, their families, students, and general-interest readers.

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

We write simply, but with care for accuracy
CET is for clinicians, support staff, and administration.

We are a nonprofit, 501(c)(3) charitable foundation led by fellow clinicians, researchers, and mental health educators and advocates.
The team thanks...

...and our hundreds of research volunteers since 1983