



# DAWN to dusk

**Chris Aiken, MD**

Instructor, Wake Forest University Dept of Psychiatry  
Director, Mood Treatment Center

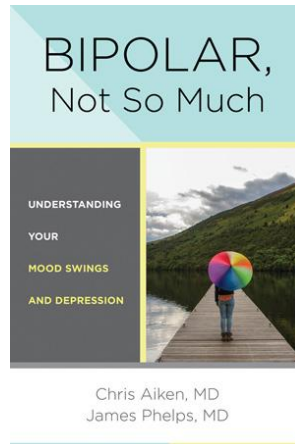
NCPA, 2018

## Disclaimer

Materials that are included in this course may include interventions and modalities that are beyond the authorized practice of mental health professionals. As a licensed professional, you are responsible for reviewing the scope of practice, including activities that are defined in law as beyond the boundaries of practice in accordance with and in compliance with your professions standards.

## Conflicts of Interest

Book royalties, *WW Norton*



# Blue light

Blue light (460-480 nm) → Melanopsin receptors in eye →  
Suprachiasmatic nucleus → Pineal gland →  
Shut down Melatonin → Awake and alert



# Sleep Inertia

- Sound alarms wake us from deep sleep 90% of the time, causing *sleep inertia*.
- This groggy state lasts 15 minutes in most people, but up to 4 hours during depression.



# Dawn Simulator

## **TURNS ON**

Gradually over 30-60 minutes to 250

## **IMPROVES**

Depression  
Sleep quality  
Cognition

## **EXAMPLES**

PER2LED  
LightenUp

?Apps (*Rise & Shine*,  
*Lichtwecker* )



# Dawn Simulation

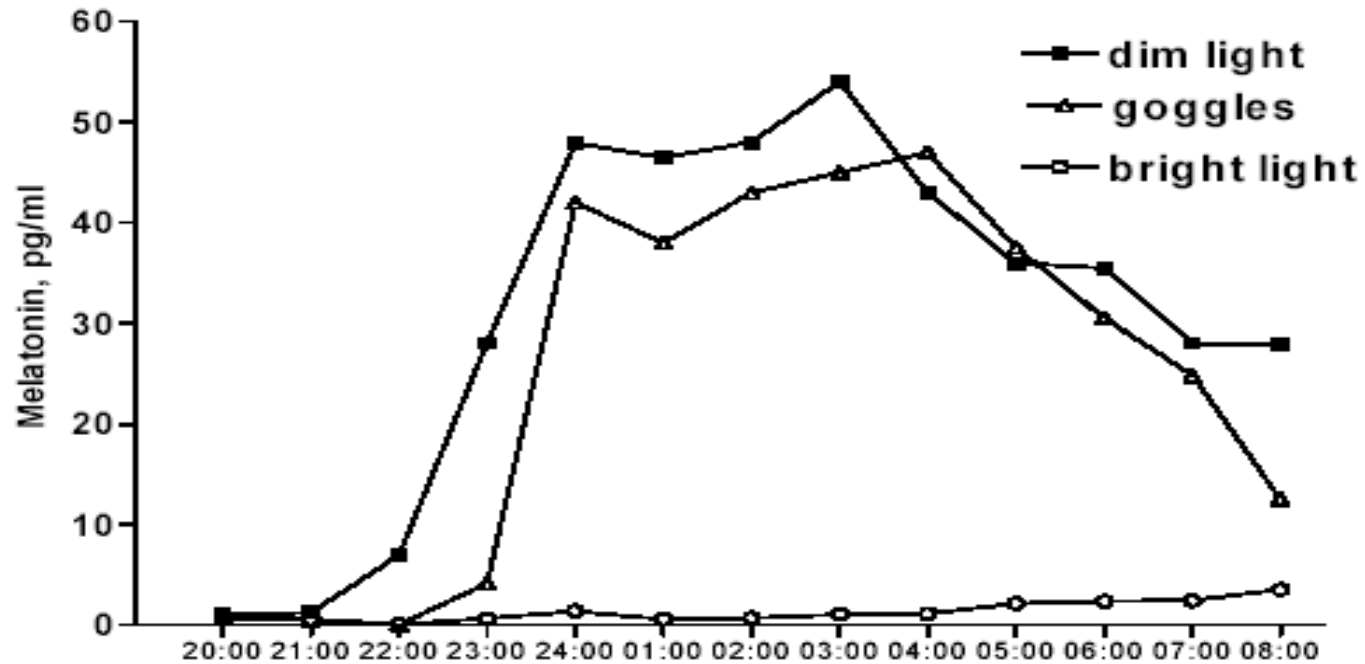
## **Evidence in Seasonal Affective Disorder (SAD)**

- Positive in 8/10 small controlled trials (total n=446)
- 7/10 of those are placebo-controlled

## **Studied in other conditions**

- SAD in recovered alcoholics
- Sleep quality in normal adults (cross-over study, n=100)
- Attention, alertness, and working memory in adolescents and sleep deprived adults (pb-control)

# Melatonin Rises with Dim Light or Blue-Light Filtering Glasses



# Light at Night (LAN)

Obesity

Diabetes

Cancer (breast, prostate)

Cardiovascular disease

Neurologic diseases

Gastrointestinal ulcers

Adverse reproductive outcomes





# Light at Night (LAN)

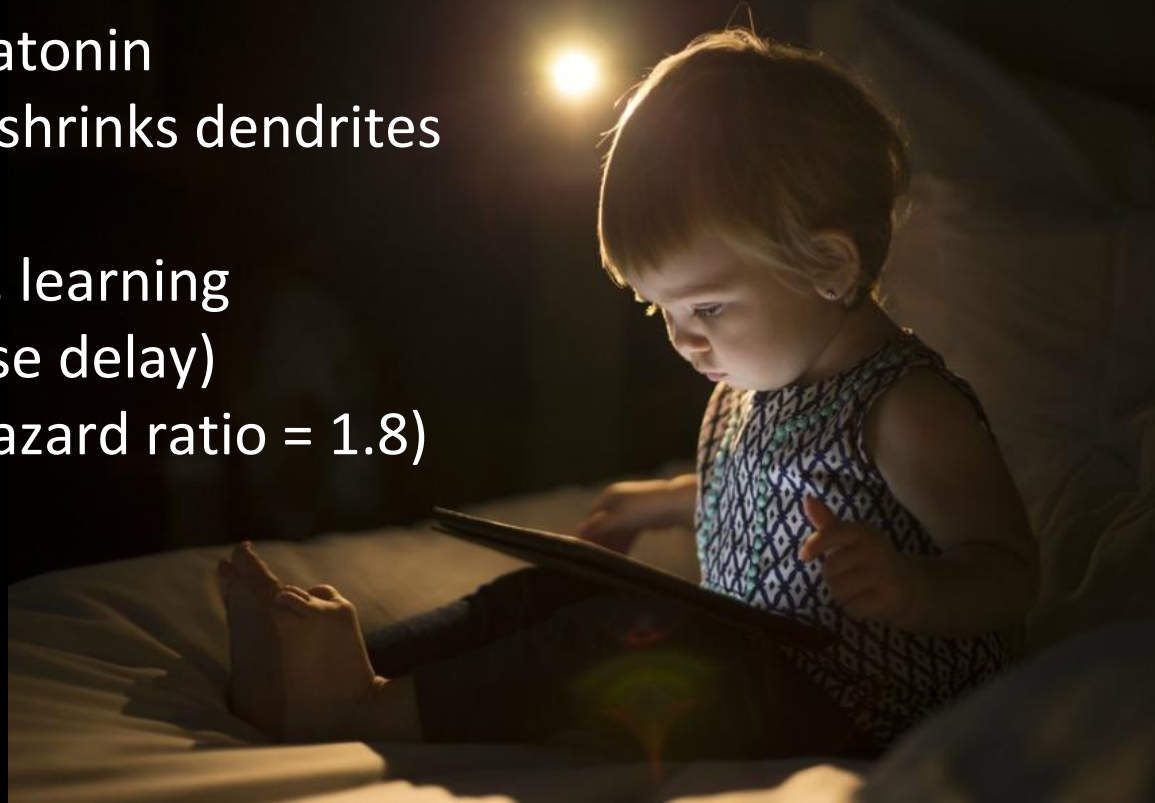
Delays and reduces melatonin

Impairs neuroplasticity, shrinks dendrites

Impairs sleep, cognition, learning

Creates night-owls (phase delay)

Increases depression (Hazard ratio = 1.8)



# Even dim light...

Longitudinal study of 863 older adults:  
Bedroom light above 5 lux was associated with  
elevated rates of depression at 2 years follow-up;  
effect was greater at higher illuminations

(Obayashi, 2018)



# Lux

Full moon	0.3
Twilight	5-10
Dark public area	20-50
Living room	50
Dark overcast day	100
Office lighting	320-500
Sunrise/set	400
Overcast day	1,000
Full daylight	10,000-25,000
Direct sunlight	32,000–100,000

# Dark Therapy

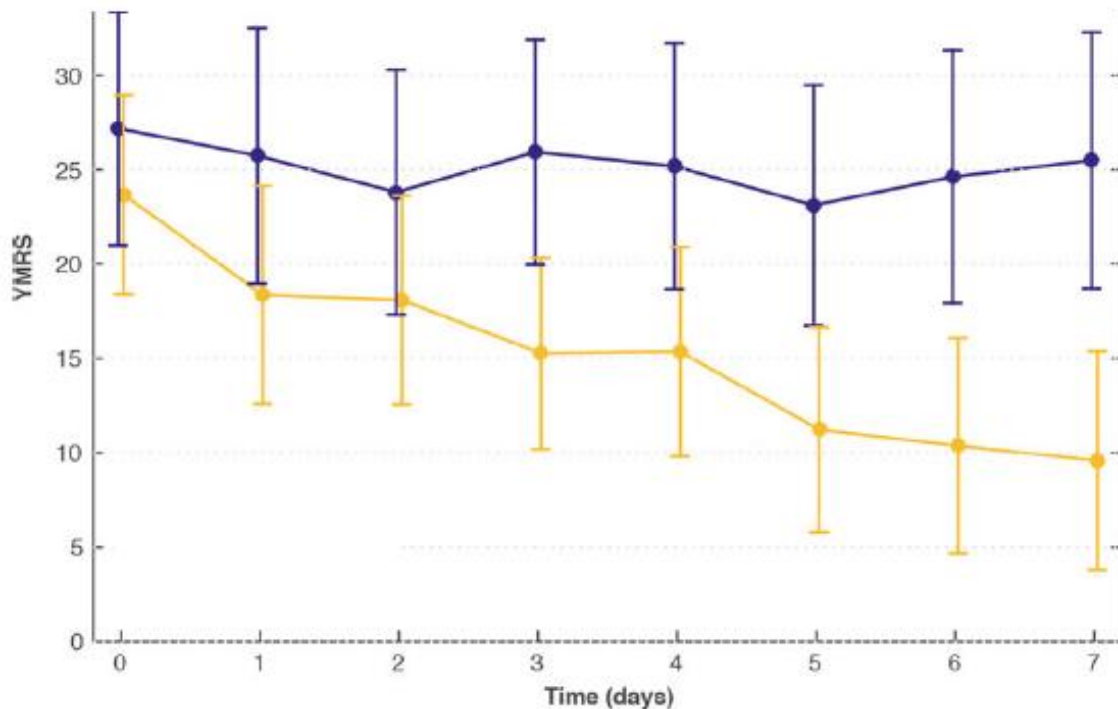


# Dark Therapy Treats

- Mania (controlled trial)
- Rapid cycling (case series)
- Shift-work syndromes (case series)
- Insomnia (controlled trial)



Dark therapy improved mania in hospitalized patients.  
Effect size = 1.8 (3-times greater than most meds).  
Patients recovered without necessarily sleeping more.



Henricksen et al. *Bipolar Disorders*, 2016

# Protocol

## 6pm to 8am

- Virtual darkness (blue-light filters) when out of bed
- Total darkness (or eye mask) when in bed
- Can start later if improved for a week or if symptoms are mild (e.g. 2 hours before bed, shifting later by 1 hour every 2-3 days)



# Glasses



Uvex Ultraspec 2000,  
S0360X , \$7 on Amazon



Uvex Skyper 3S1933X  
\$7-10 on Amazon



Lowblue.com  
\$70-80



# Black out

- Blackout curtains (such as ShiftShade, or buy blackout fabric, attach with pins or Velcro)
- Aluminum foil against window
- Electric tape over LED lights
- Sleep in basement

## **Low blue nightlights:**

- Maxxima MLN-16 Amber LED Night Light Plug
- SCS Nite-Nite Light Bulb or Sleep-Ready Light
- [lowbluelights.com](http://lowbluelights.com), [somnilight.com](http://somnilight.com)
- Apps: f.lux, Apple Nightshift mode, Kindle Candle



# Blue Light Filters

## Computers

Windows: f.Lux

Mac: *Candlelight* by Oliver Denman

## Smartphones, Tablets

Apple *Nightshift mode*

Kindle *BlueShade*

Android *Twilight* and *Blue Light Filter* app

# BRIGHT LIGHT AND CHRONOTHERAPY FOR MOOD DISORDERS

Thomas M Penders MS, MD

Walter B Jones Center

Affiliate Professor, East Carolina University

North Carolina Psychiatric Association Annual Meeting – September, 2018

# DISCLOSURES

Presenter has no material financial conflict to disclose.

# CHRONIC DISEASE CARE

- CDC reports that 86% of the \$2.3 trillion dollar annual health care expenditure directed spent on treatment of chronic disease
- Often chronic illnesses affected by lifestyle patterns that are modifiable.
- Among solutions to the problems of managing chronic illness is for greater patient engagement in their care.

# AFFECTIVE DISORDERS

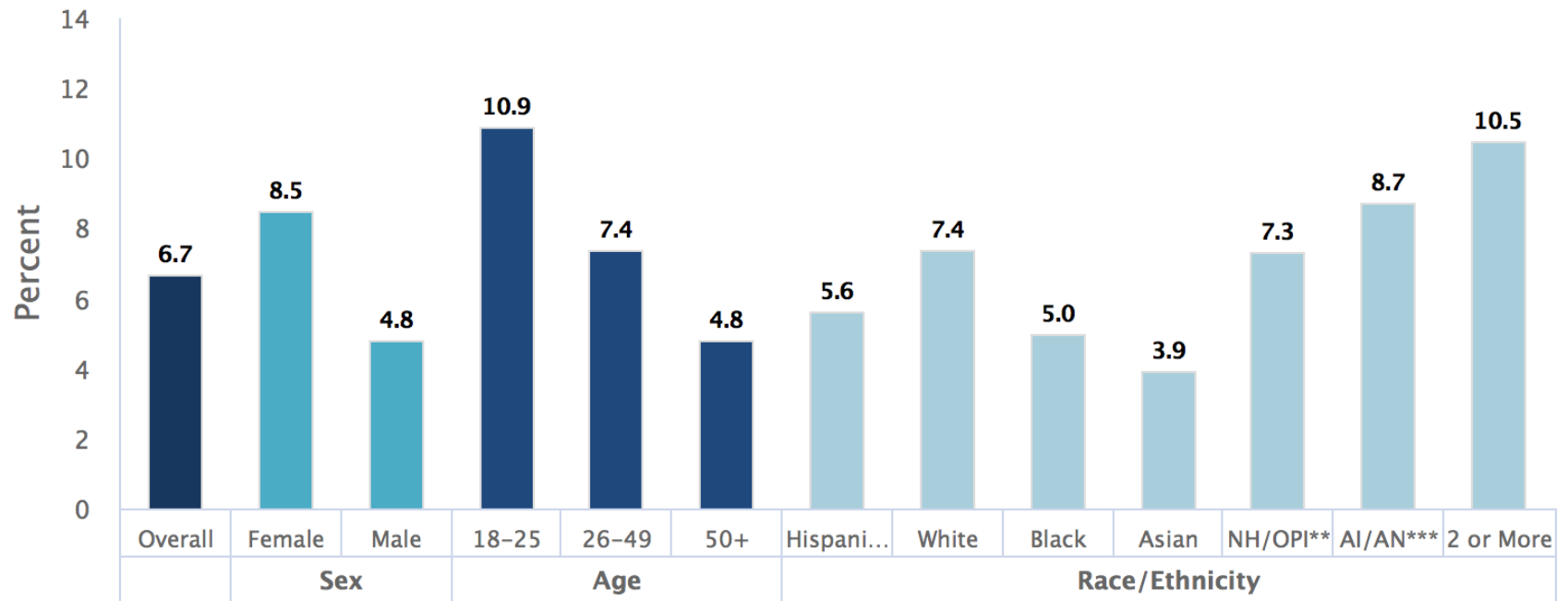
- Among the most disabling of chronic diseases
- Low adherence to treatment recommendations
- Limited efficacy for treatment
- Common association with chronic medical illnesses



# MAJOR DEPRESSIVE DISORDER

Past Year Prevalence of Major Depressive Episode Among U.S. Adults (2016)

Data Courtesy of SAMHSA



?



Photo: A. Mahmoud

Jeffrey C. Hall



Photo: A. Mahmoud

Michael Rosbash

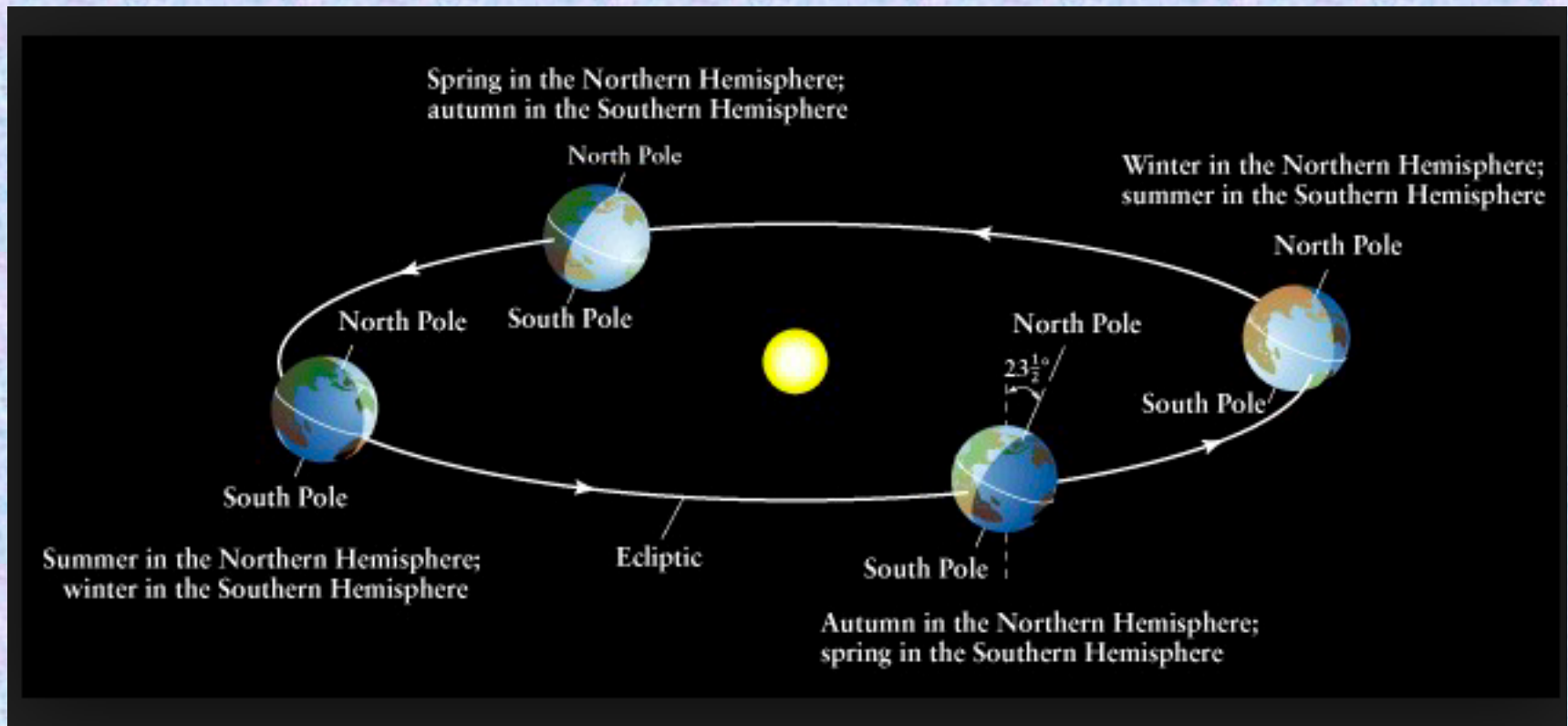


Photo: A. Mahmoud

Michael W. Young



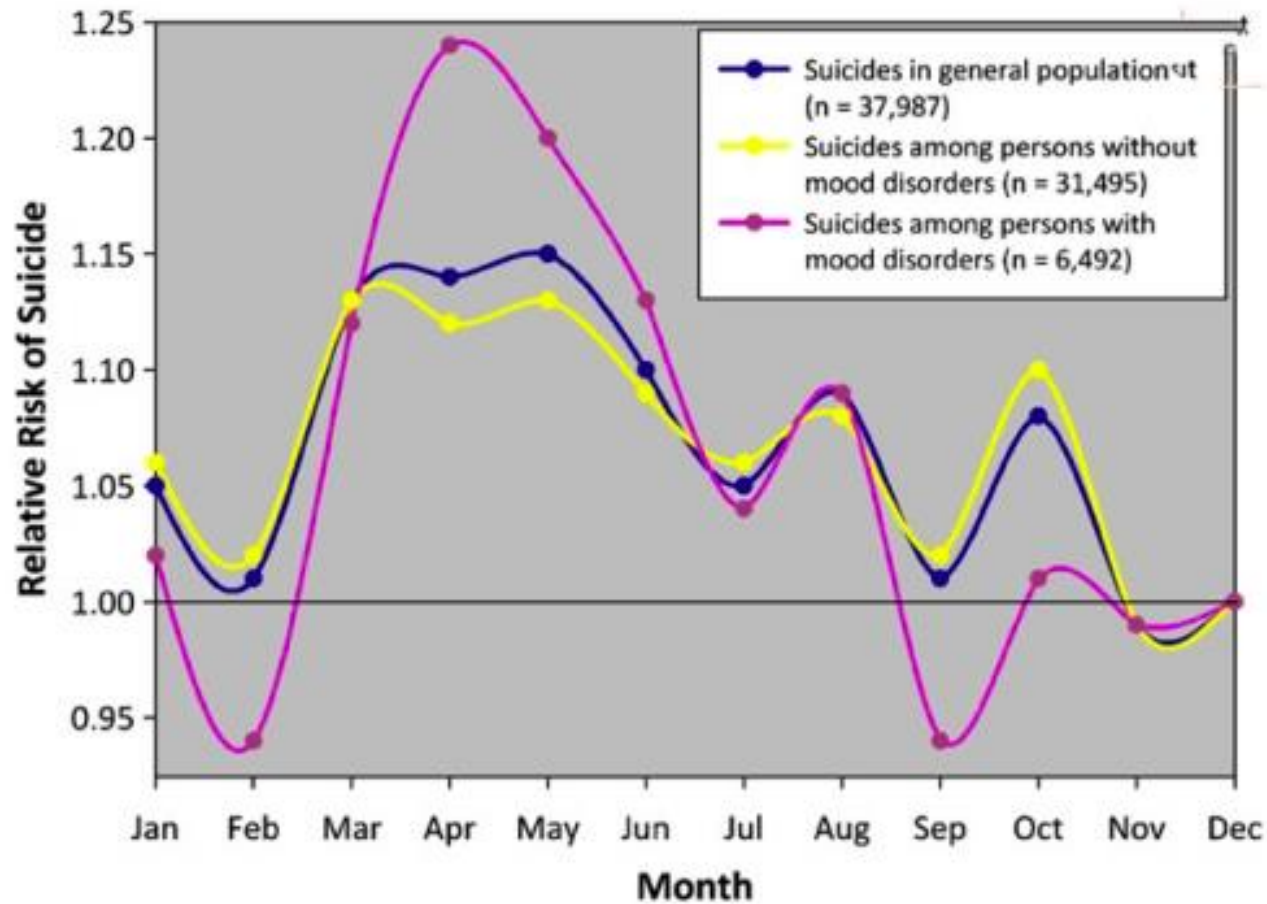
# SEASONAL VARIATION IN SUNLIGHT



# SEASONAL AFFECTIVE DISORDER

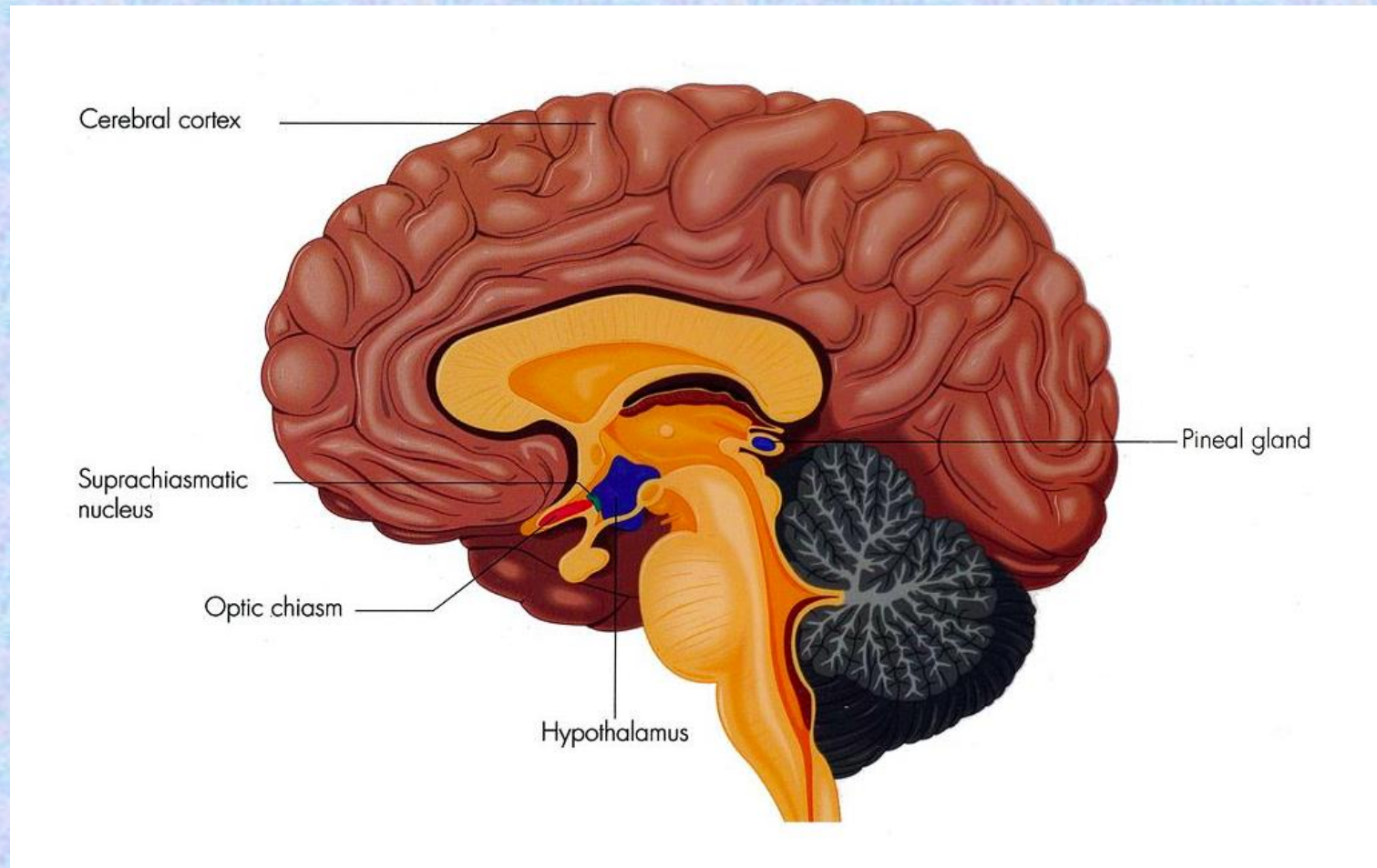
- 1980 – Lewy shows melatonin suppression by light
- 1984- Rosenthal and others published the first study demonstrating efficacy for exposure to bright lights BLT) for Seasonal Affective Disorder(SAD).
- Studies show efficacy in shift work disorders, jet lag, bulimia, dementia, sleep disorders

# SUICIDE RATES BY MONTH





# NEUROPHYSIOLOGY OF DIURNAL RHYTHMS

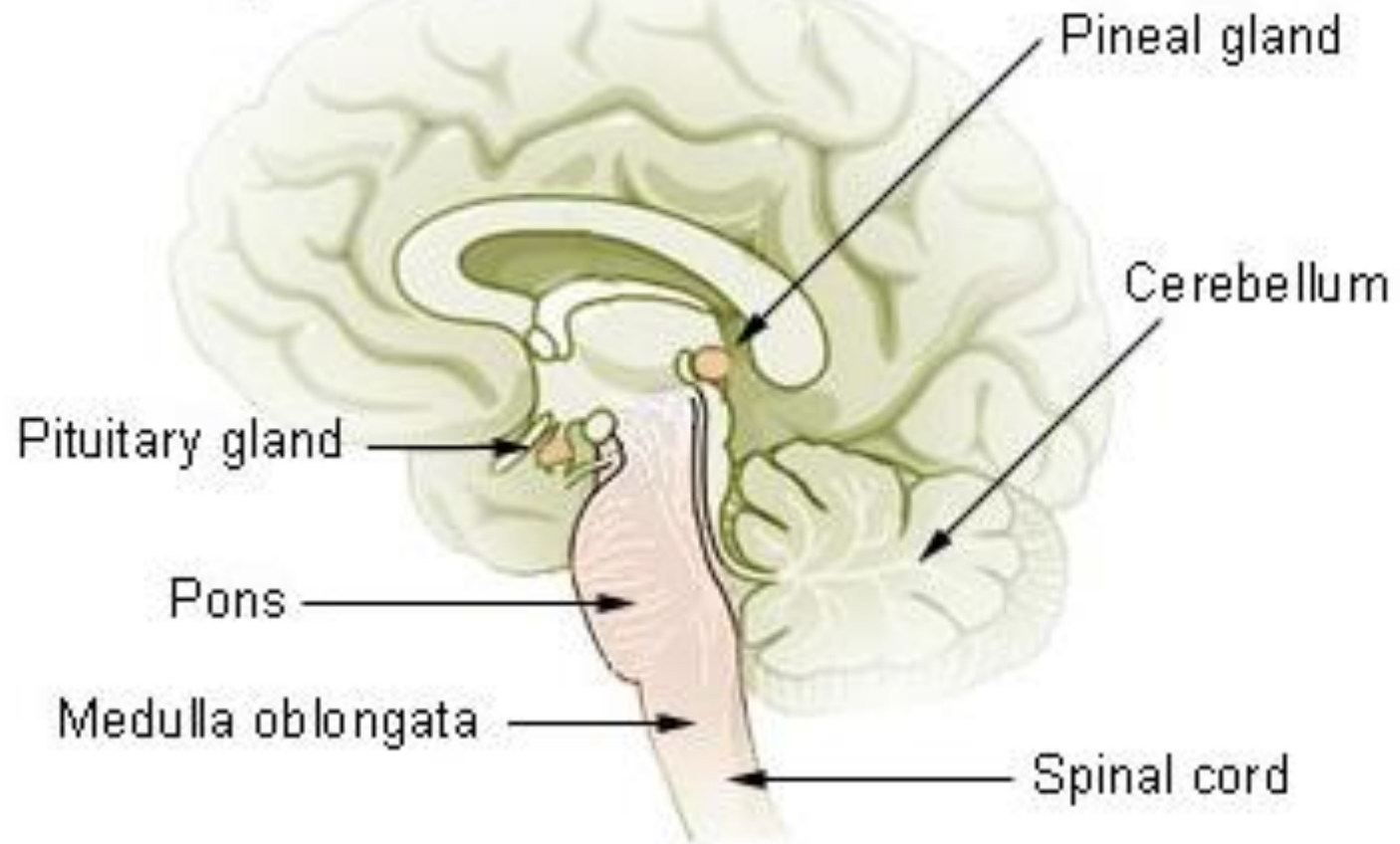


# Suprachiasmatic Nucleus

- Diurnal pacemaker
- 10-50,000 neurons
- Information on dark-light by way of retinal melanopsin
- Connects by way of serotonergic neurons to Pineal; feedback from pineal by MT neurons
- Diurnal changes eliminated in animals where SCN is ablated

# PINEAL GLAND

## **Pituitary and Pineal Glands**





# MELATONIN

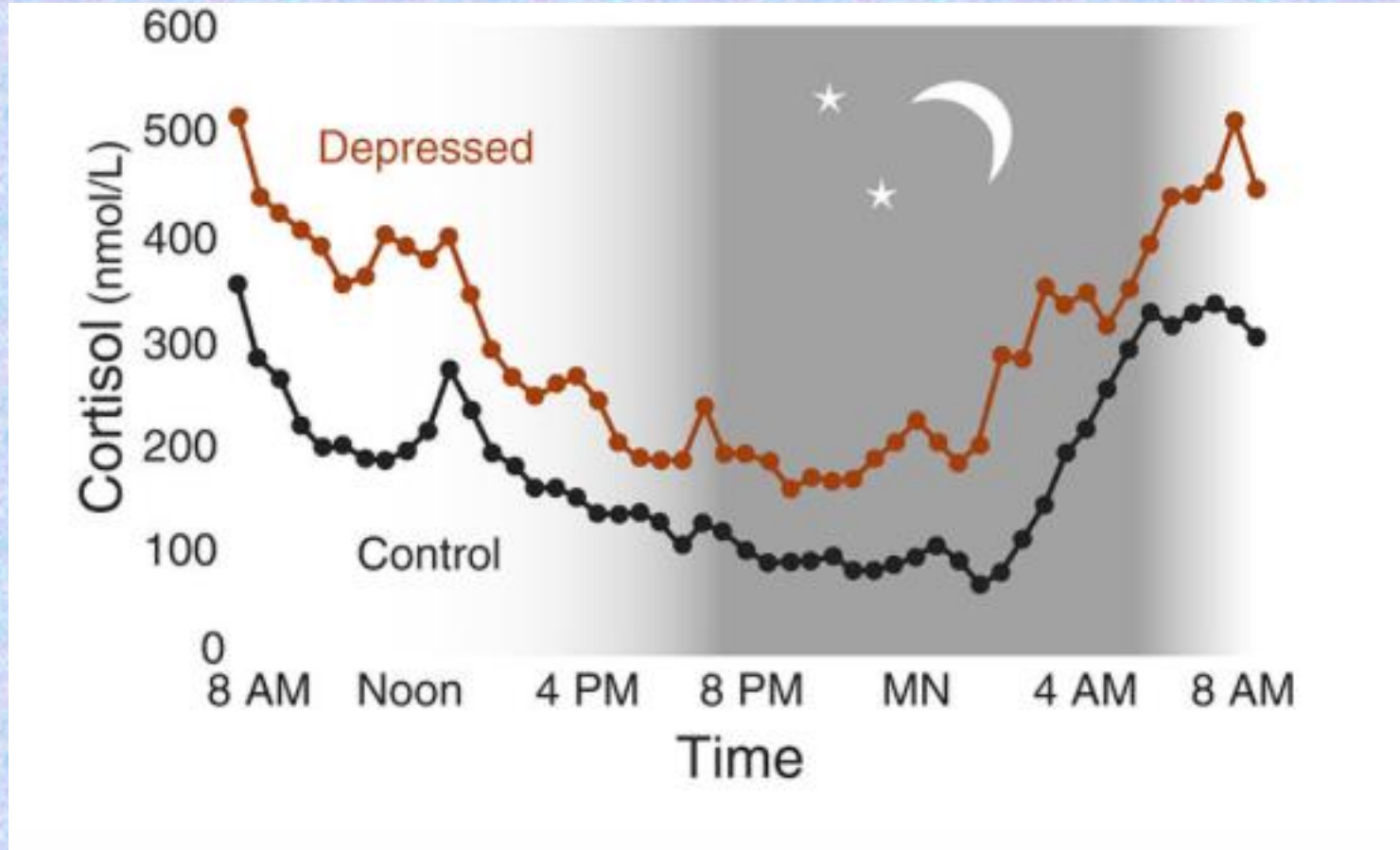
- Secreted by the Pineal in specific circadian pattern – high at night and low during daylight
- Synthesized from its precursor, Serotonin
- Pace of secretion controlled by the SCN
- Rapidly distributed throughout the body influencing any number of biological function
- Connections to paraventricular nucleus with connections to sympathetic system and pituitary

# RHYTHMICITY IN CENTRAL SEROTONIN

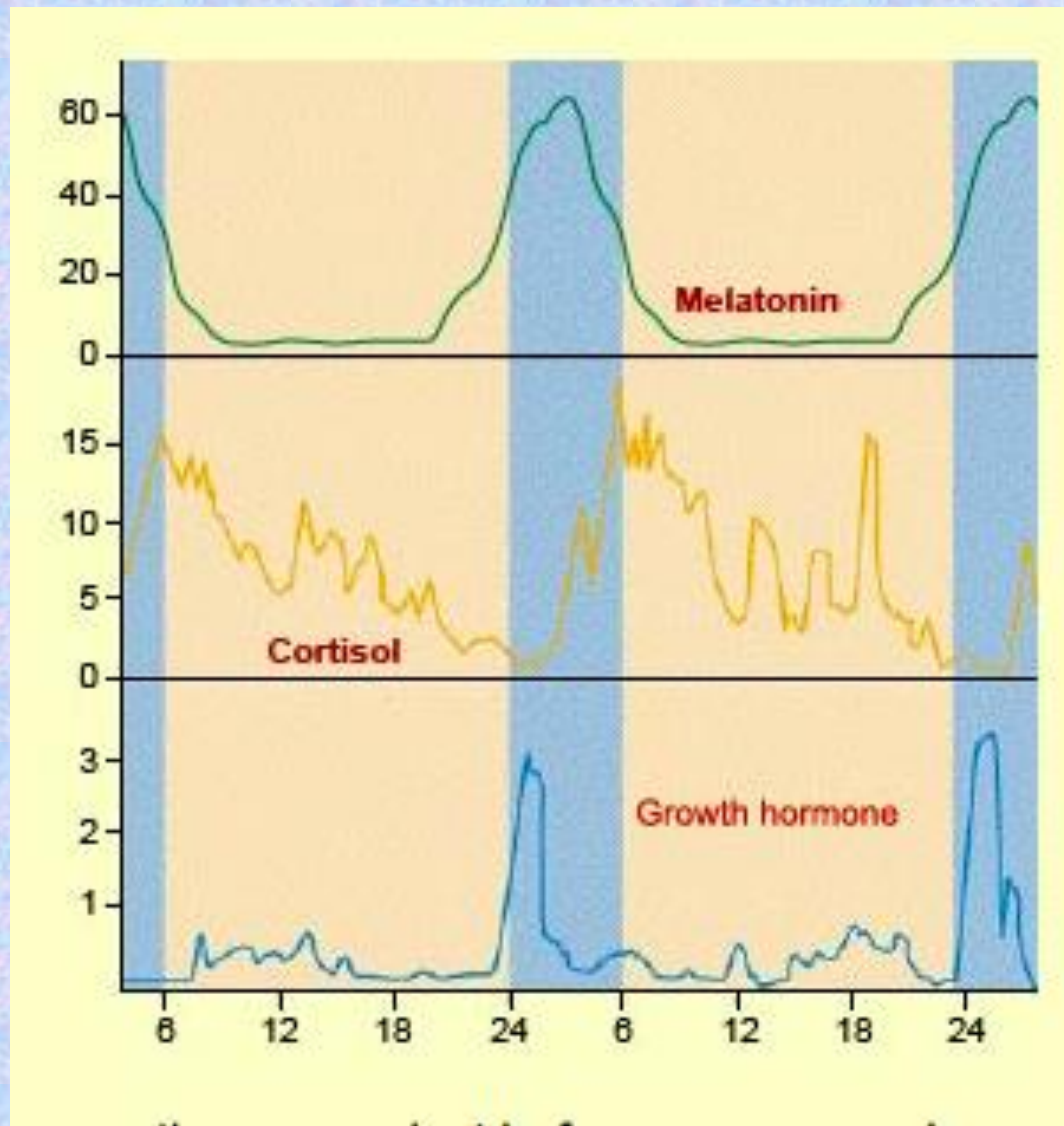
- Serotonin – seasonal changes in brain levels and turnover
- 5HTT binding varies as much as 40% in association with season
- Highest 5HTT binding occurs during winter months with lowest around the summer solstice



# HUMAN DIURNAL RHYTHMS



# HORMONES



# DIURNAL BODY TEMPERATURE



Adapted from: Gerry Wyder



# CHRONOBIOLOGY OF AFFECTIVE DISORDERS



# MORNINGNESS-EVENINGNESS QUESTIONNAIRE

- 19 multiple choice questions
- What time would you get up if you were entirely free to plan your day?
- 12. If you got into bed at 11:00 PM, how tired would you be?
- 17. Suppose you can choose your own work hours. Assume that you work a five-hour day (including breaks), your job is interesting, and you are paid based on your performance. At what time would you choose to begin?

# SEASONAL MOOD VARIATION IN NON-CLINICAL POPULATION

- The Morningness Group had a lower BSDS score than both the Eveningness and Intermediate Groups.
- The Eveningness Group had significantly higher BSDS-D scores than either the Morningness or the intermediate group.
- The Eveningness Group had significantly higher BSDS-M scores than the morningness group.
- The Eveningness may be more related to mood fluctuation than the morningness.
- Eveningness may be an important factor related to mood fluctuation or soft bipolarity.



# DIM LIGHT MELATONIN ONSET (DLMO)

- Precise measure of chronotype
- Defining measure for delayed-phase sleep disorder
- Available by serum, saliva or urine
- Sampled 3 times in dim light, at 30 minute intervals; based on estimation from MEQ or predictions from temperature
- Determine timing of BLT for several disorders. Sleep onset 2 -3 hours after DLMO

# MEQ ASSOCIATIONS

- Study of identical and fraternal twins suggested that 54% of variance heritable
- Gender differences in association with anxiety and depression
- Eveningness associated with greater novelty seeking, lower impulse control and self-regulation
- Eveningness associated with reports of poorer general health

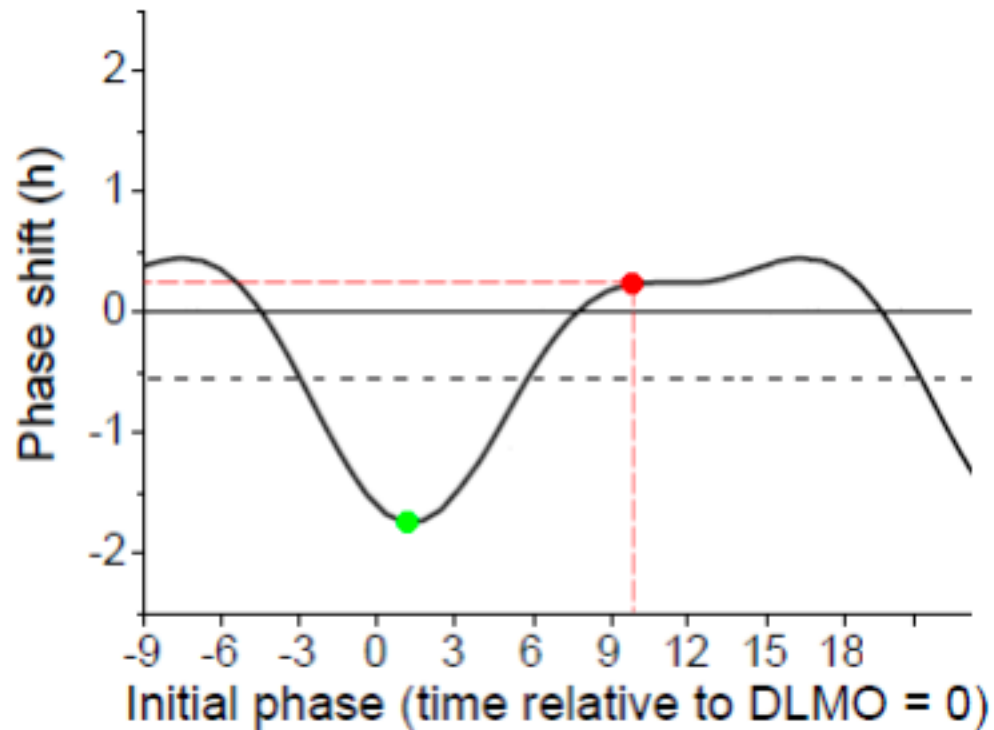


# CHRONOTYPES AND AFFECTIVE DISORDERS

- Meta-analysis of 36 studies involving 15,734 patients concluded:
- Mild association between “eveningness” and depression particularly with severity
- Interventions into circadian disruptions are often helpful in management

Au J, Reece J. The Relationship between chronotype and depressive symptoms: a meta-analysis. *Jour of Affect Dis.* 2017;218:93-104

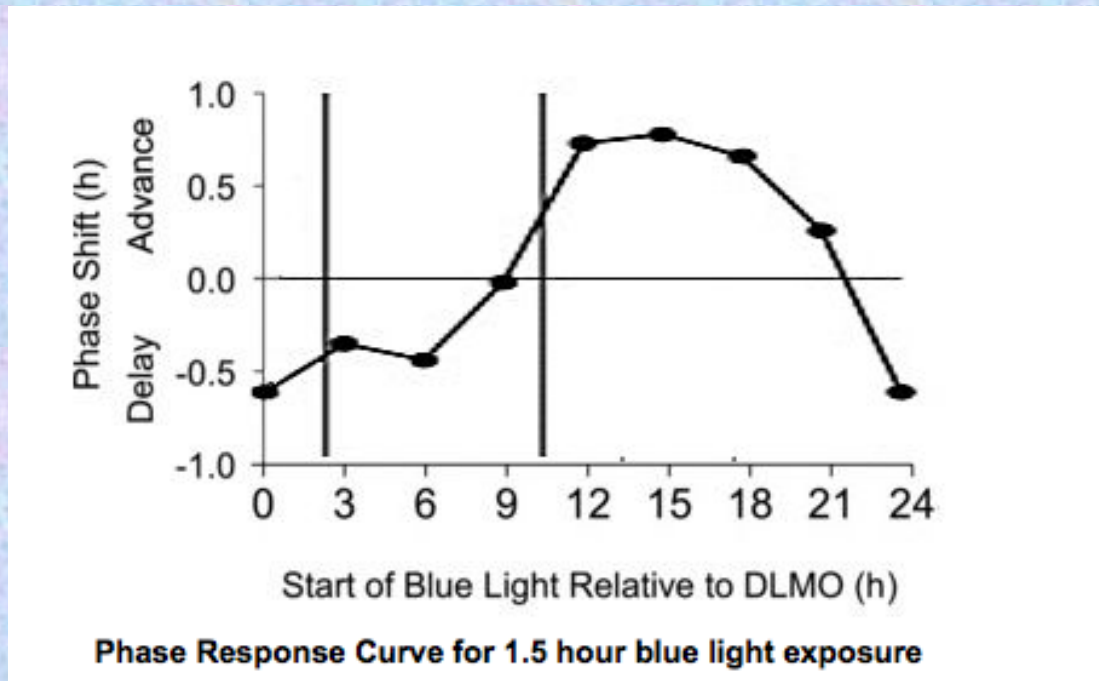
# PHASE RESPONSE CURVE



**Phase Response Curve for 1 hour white light exposure**

# PHASE SHIFTS

- Phase advance (earlier DLMO and sleep onset) with morning light
- Phase delay (later DLMO and sleep onset)



# SEASONAL AFFECTIVE DISORDER

- Prototype for chronobiological disturbance
- Rosenthal et al described a subset of depressive disorders with annual recurrence and spontaneous remission
- Sub-syndromal mood fluctuations in the general population
- Prevalence varies with latitude; 1% FL, 9% Alaska
- Number are phase-delayed
- Bright Light therapy in AM is first line Rx



# BRIGHT LIGHT THERAPY

- Applied using a light box containing fluorescent lamps.
- Various models available
- Light intensities of 5000-10,000 Lux
- Begin with 30 minutes
- Morning administration appears to have some advantage
- Effects of treatment do not last beyond exposure
- Onset of therapeutic effect – 3 to 7 days

# LIGHT BOX



# OTHER BRIGHT LIGHT SOURCES



BLT Ambient light. Looking into light not recommended



# BLT INOVATION



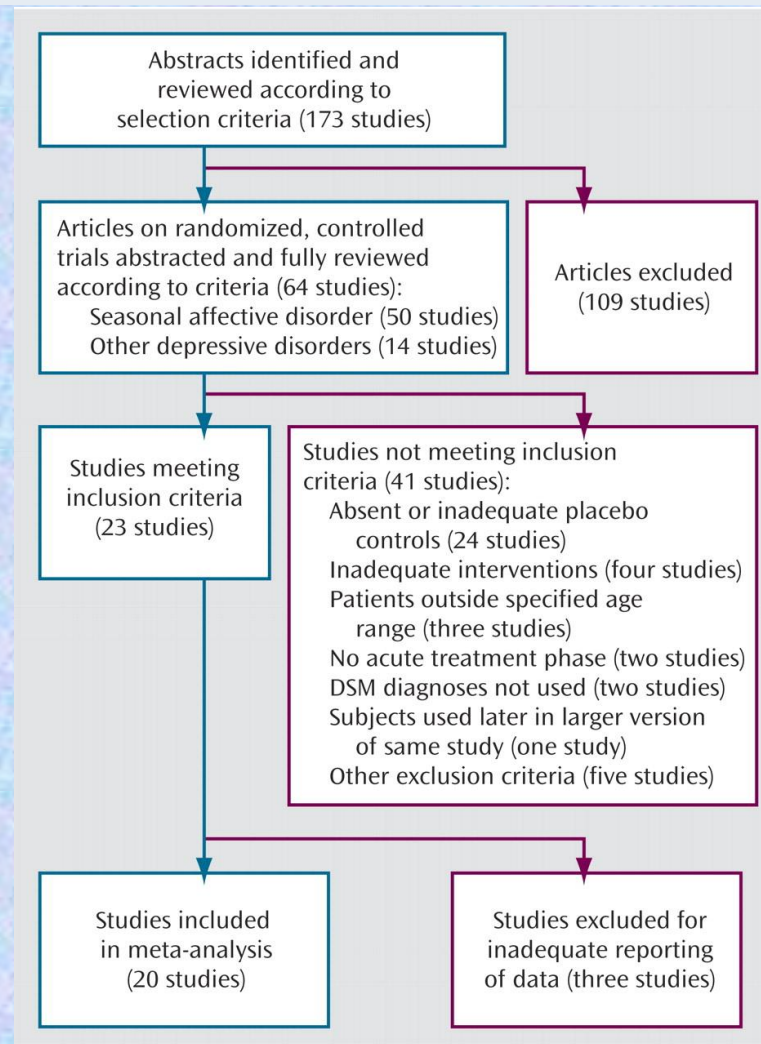


# NONSEASONAL DEPRESSION

- Meta-analysis by Golden et al (2005)
- 20 studies
- Served as basis for APA recommendation for BLT for both seasonal and non-seasonal depression
- Effect sizes equivalent to those for antidepressant pharmacotherapy

Golden RN et al. The Efficacy of Light Therapy in the Treatment of Mood Disorders: A Review and Meta-analysis of the Evidence. Am Jour Psych. 2005;Apr.

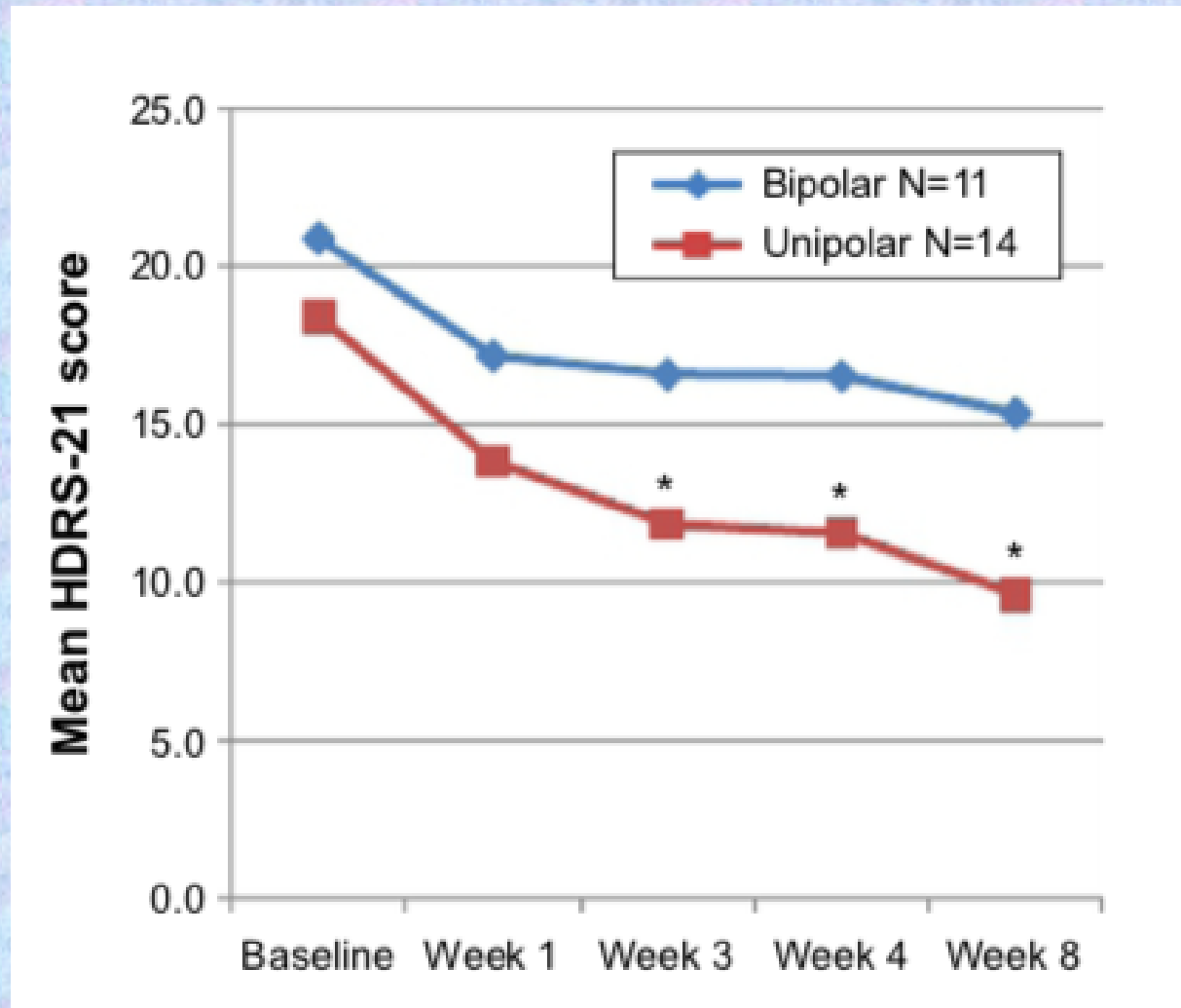
## From: The Efficacy of Light Therapy in the Treatment of Mood Disorders: A Review and Meta-Analysis of the Evidence



# CONCLUSION OF GOLDEN REVIEW

- Meta-analyses revealed that a significant reduction in depression symptom severity was associated with bright light treatment
- Eight studies, having an effect size of 0.84 and 95% confidence interval [CI] of 0.60 to 1.08)
- Dawn simulation in seasonal affective disorder (five studies; effect size=0.73, 95% CI=0.37 to 1.08) and with bright light treatment in non-seasonal depression (three studies; effect size=0.53, 95% CI=0.18 to 0.89).
- Bright light as an adjunct to antidepressant pharmacotherapy for non-seasonal depression **was not effective** (five studies; effect size=-0.01, 95% CI=-0.36 to 0.34).

# BLT Augmentation in TRD

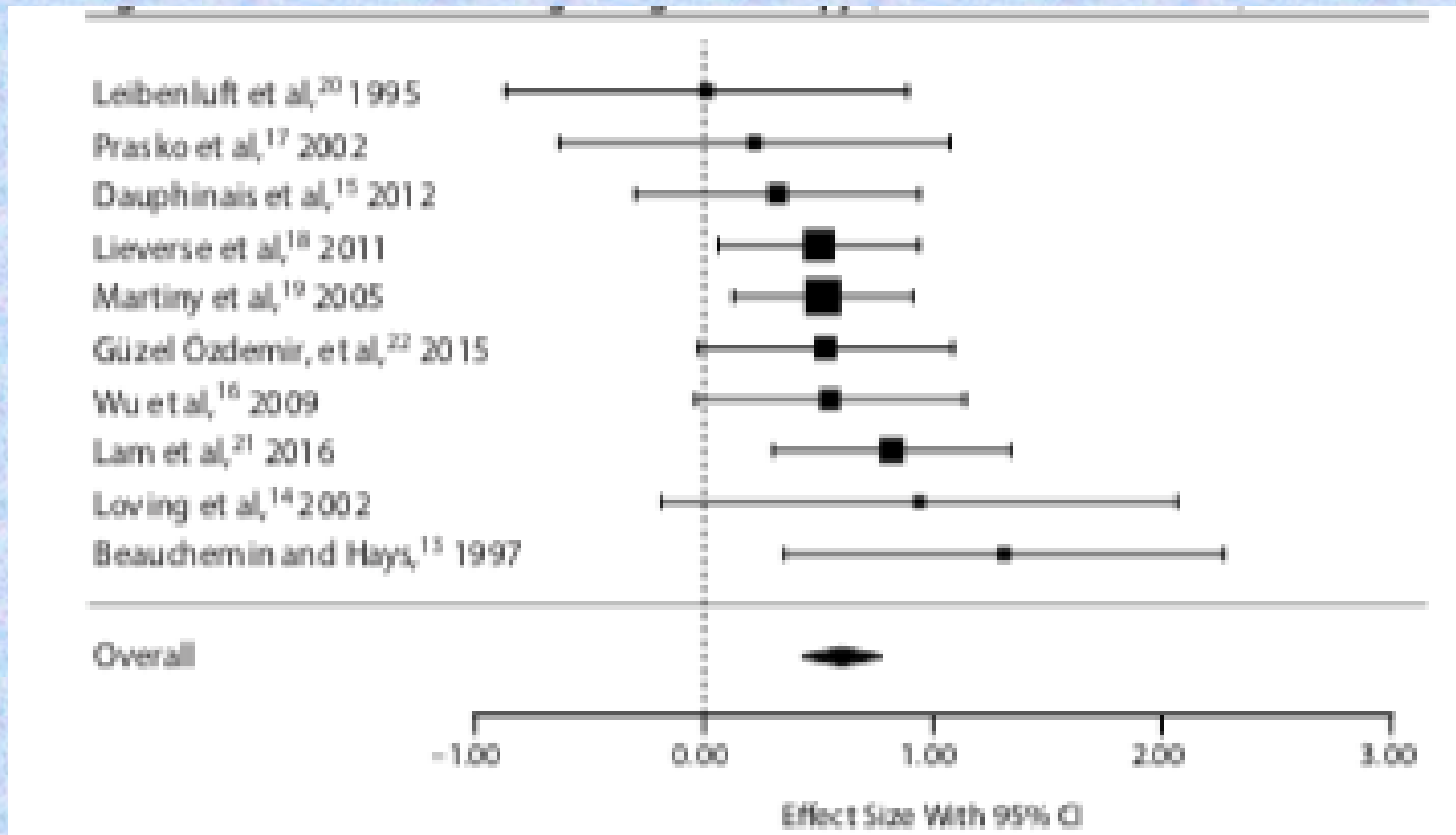


Camardese G et al. Augmentation of light therapy in difficult to treat depressed patients. *Neuropsych Dis and Treat*. 2015;11:2331-38



# BLT AUGMENTATION

EFFECT SIZE FOR EACH BLT STUDY. > 0 FAVORS TREATMENT



# BLT in bipolar disorder

- Robust response in bipolar depression
- Can precipitate mania/hypomania
- Dosage of light has been titrated against emergent symptoms
- Some may develop mixed state
- Use of sleep deprivation, phase advance, mood stabilizers and antidepressants hastened response



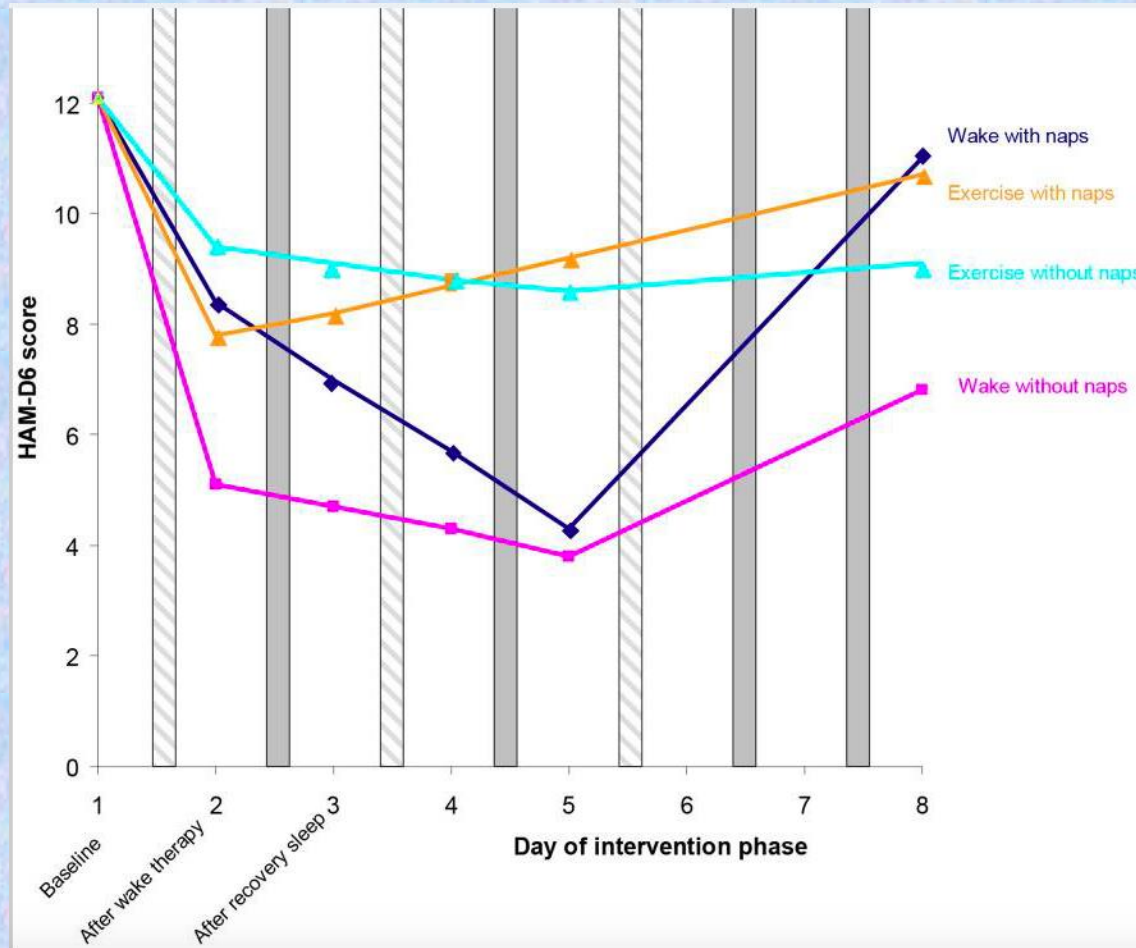
# SLEEP DEPRIVATION

- In the 70s observation that depressed individuals cycling through the night had a rapid antidepressant response in about 50%
- Effect mostly disappears upon return to sleep
- Multiple efforts to preserve initial effect have met with some success

# WAKE THERAPY

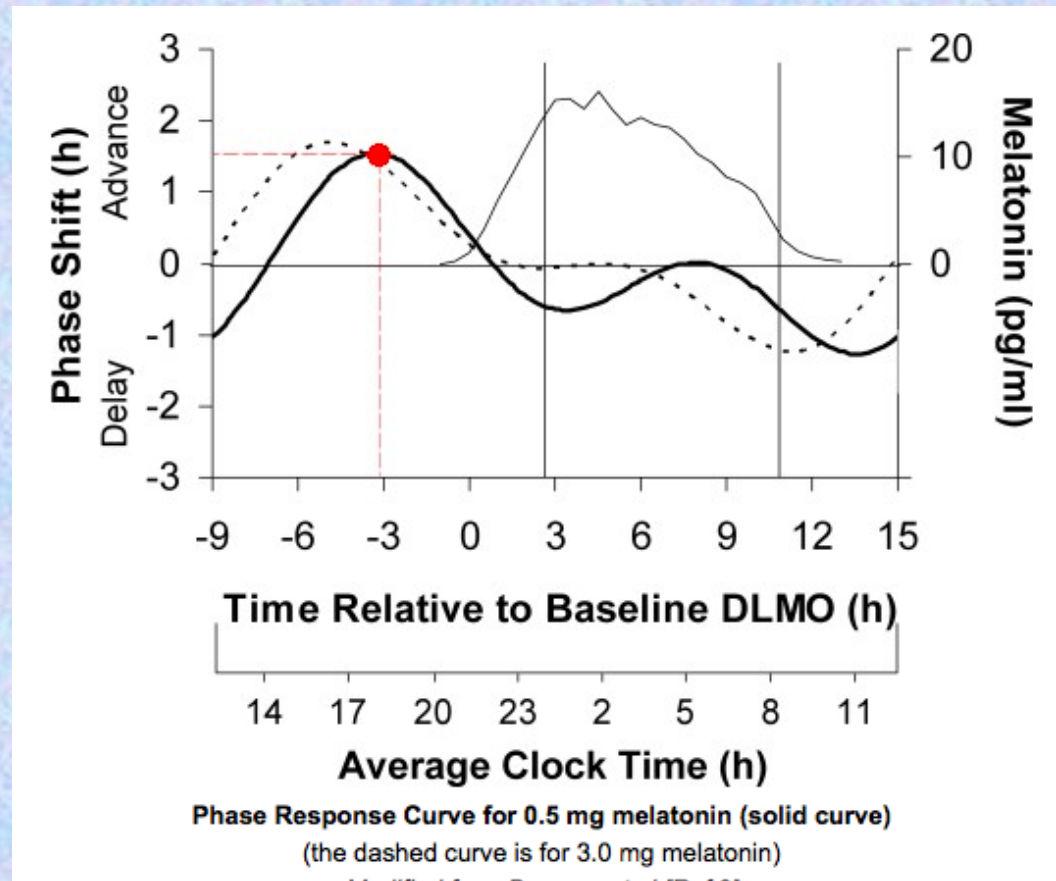
- Maintaining wakefulness while instituting interactions to maintain effect:
- Lithium
- Bright Light Therapy to produce phase advance
- Antidepressants

# EFFECTS OF WAKE THERAPY



# PHASE ADVANCE INTERVENTIONS

- BLT hours prior to DLMO
- Administration of Melatonin has effect – i.e. early administration phase delay.





# OTHER APPLICATIONS FOR BLT

- Jet-lag – Use of BLT to reset timing of sleep onset can prepare individuals for travel across several time zones
- Experimental use of flashing blue light may accomplish the same
- Exposure to bright light early in a person's wake period and dim light at the end of the wake period has the effect of moving the internal clock earlier improving alertness in shift workers



# BLT SAFETY

- Adverse effects include headache, eyestrain, nausea and agitation;
- Tend to remit spontaneously or after dose reduction.
- Patients with bipolar disorder may switch to hypomania during therapy, and suicidality may sporadically occur early in the course of treatment.
- BLT can also cause menstrual irregularities.
- Since retinal degeneration can occur in patients with a family or personal history of retinal damage, patients should consult an ophthalmologist before initiating treatment

# LIGHT IN ARCHITECTURAL DESIGN

- Recognition by American Institute of Architects that natural light has health consequences for:
  - Libraries
  - Schools
  - Hospitals
  - Office buildings

# CONCLUSION

- Bright Light Therapy can be an effective adjunctive intervention for treatment of depressive disorder
- Sleep deprivation combined with morning BLT can accelerate response to antidepressant treatment
- Melatonin onset may be a biomarker for depressive disorders predictive of response to BLT.

# DISCUSSION