Sleep/Wake Rhythms & NeurOptimal

Ed O'Malley, PhD, FAASM

Diplomat, American Board of Sleep Medicine
Zengar Certified Master Neurofeedback Trainer
Optimal Sleep/Optimal Neurofeedback
Great Barrington MA ¤ *eddom7@gmail.com*

Insomnia Consultant, Sleep HealthCare of CT
Fairfield CT ¤ *eomalley@sleephealthcarect.com*

What are Natural Sleep Rhythms

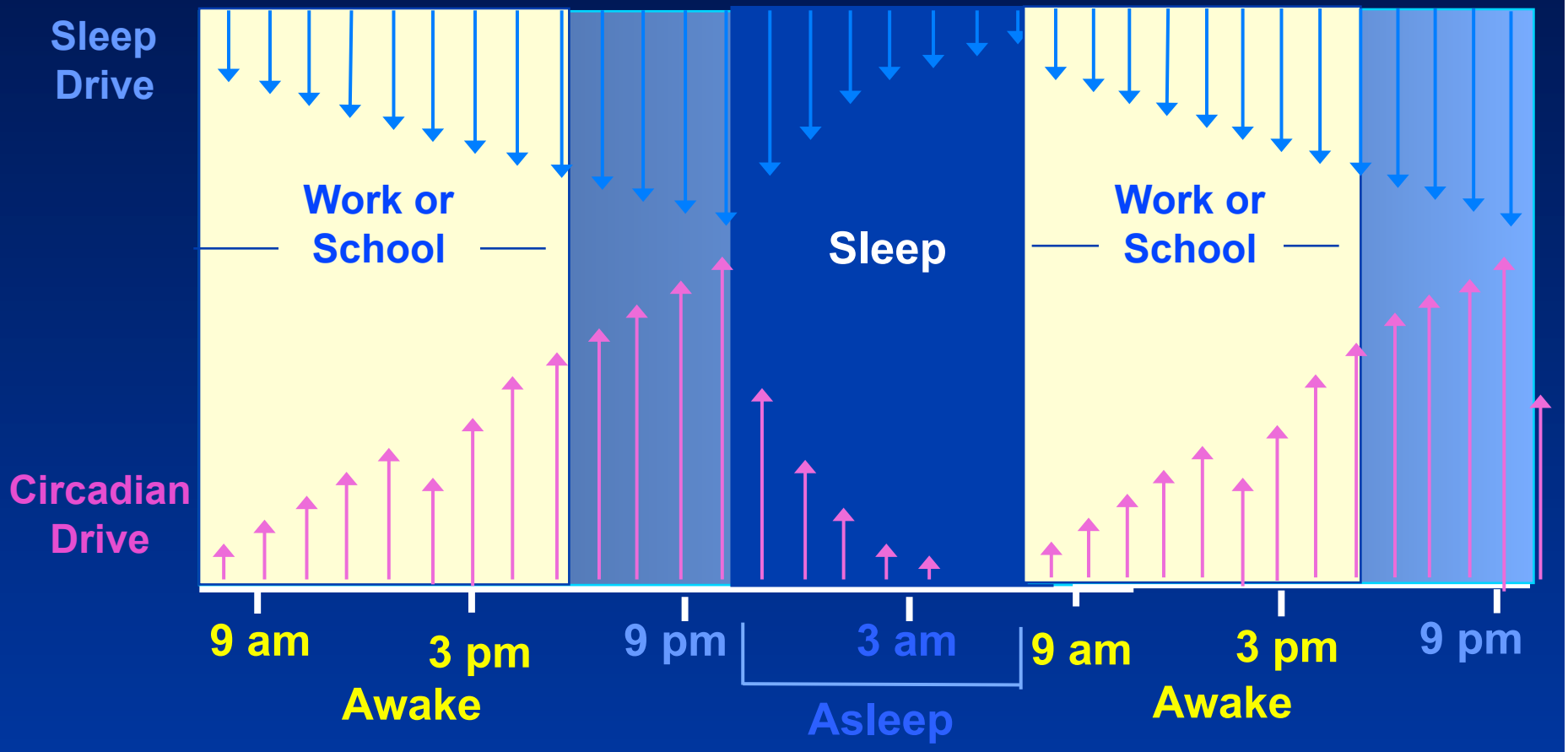
1. Biological/Circadian Factors
    a) Sleep Drive
    b) Wake Drive (Circadian)

2. Behavioral (Habitual) Patterns
    a) Traditional/Indigenous cultures
    b) Western society
        a) Preindustrial
        b) Postindustrial (nocturnal light)

What is a Circadian Rhythm?

1. Comes from “circa” meaning “near” and “dia” meaning “day”
2. Responsible for establish a 24 hour cycle that responds daily to seasonally changing daylight
3. Also transduces light into healthful benefits

Sleep Rhythms:
Sleep Drive and Circadian Drive



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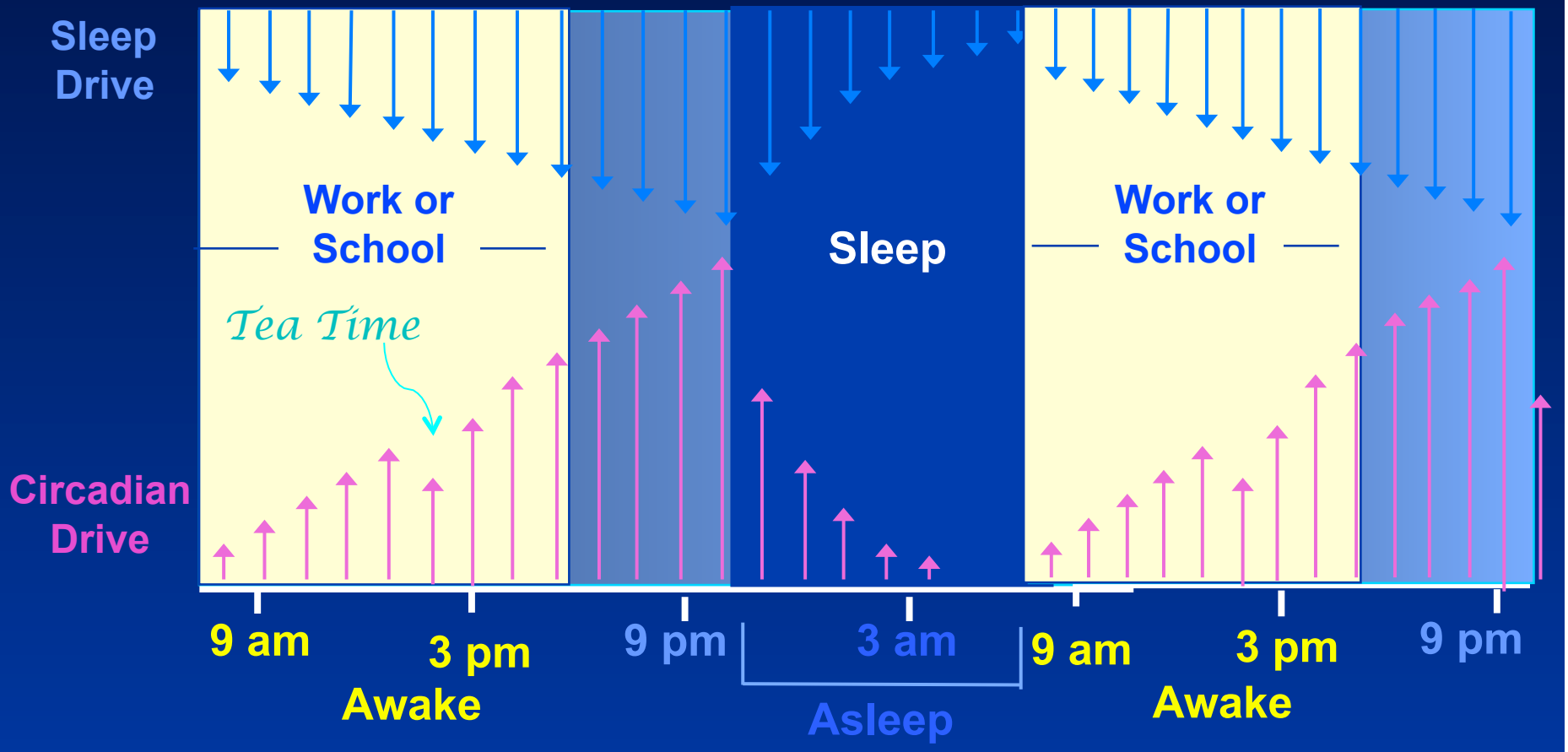
Sleep Rhythms:
Sleep Drive and Circadian Drive



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What is a Behavioral Rhythm?

1. Something we do consciously
   a) Activities performed, repeatedly, regularly-eg, put on PJs, brush teeth, adjust thermometer, go to bed, get up, eat, go to work
2. Or, something we do subconsciously
   a) Can become habitual pattern of activity, way of being, thinking, doing etc-eg, daily drive to work same route-hardly notice; walking, jogging

Habitual Patterns: Native Cultures

1. Until recently, the entire family would arise with the sun
    a) Daily sleep wake rhythm
    b) Consistent with circadian rhythm
    c) Consistent with Natural Rhythms
        a) Morning “blue” light, Evening “red-orange”
    d) Consistent with health
2. Bedtimes would vary loosely based on age
    a) Consistent with adequate sleep requirements cross the lifespan
3. Regular exposure to “night rhythms”
    a) Awake in the dark

Habitual Patterns: Native Cultures

Habitual Patterns: Western Culture Pre-Industrial (Before "Night Lights")

1. Sleep was broken into segments
   a) First Sleep usually from after dinner until around midnight
   b) Awake quiet time would be used for many and varied activities: reading, smoking, conversing or socializing, intimacy, meditative–like states, praying, planning for the future
2. Evidence from the NIH studies
   a) Tom Wehr kept subjects in bed, in dark for 14hr
   b) All had 1st sleep periods that were followed by quiet wakefulness—high alpha states-increased Prolactin!
3. Second Sleep usually from 1 or 2 am until dawn
   a) NIH subjects same as Victorian times

Benefits of 1st Sleep

It is of no small benefit on finding oneself in bed in the dark to go over again in the imagination the main outlines of the forms previously studied, or of other noteworthy things conceived by ingenious speculation.

LEONARDO DA VINCI

Habitual Patterns: Western Culture Post-Industrial (After "Night Lights")

1. Sleep in a single 8hr block
   a) Evidence that there is still a propensity to awaken after the first ~3-4 hours sleep
   b) This is after 2 ultradian cycles-brain has satisfied deep sleep requirement and is somewhat refreshed and capable of arousing
   c) Many attempts at finding alternative, more "efficient" sleep patterns as evidenced by "hack your sleep" protocols
2. No longer significant exposure to night darkness
   a) Disconnection from our natural exposure to light/ dark cycle
   b) Disconnection from Nature's rhythms

Habitual Patterns: Western Culture Post-Industrial (After "Night Lights")

1. We have 9-5 jobs
   a) We awaken to the alarm (mostly) regardless of biologic drive for adequate sleep
   b) We reset our circadian clock for same bedtime and get exposed to cues that awaken us
2. We have evening shifts & night shifts
   a) We *really need* to awaken to the alarm
   b) We take naps
3. We sleep in on the weekends or rearrange nights to days
   a) Reset our clocks to later times
   b) Difficulty returning to weekday work schedule

Habitual Patterns: All Cultures

1. The light dark cycle affects all life on the planet, *including* humans
2. Specifically in humans it affects metabolism (and repair), reproduction, immune function, blood pressure, and of course, the sleep/wake cycle.

World Health Org Lists Shift Work as Carcinogen (2007)

1. Nurses Long term study
   a) association with higher risk of breast cancer
2. Animal studies
   a) shows direct cause & effect of circadian disruption by light leads to cancer
3. Mechanism
   a) Melatonin suppression by light increases Estrogen

http://www.webmd.com/cancer/news/20071130/night_shift-work- may-cause-cancer

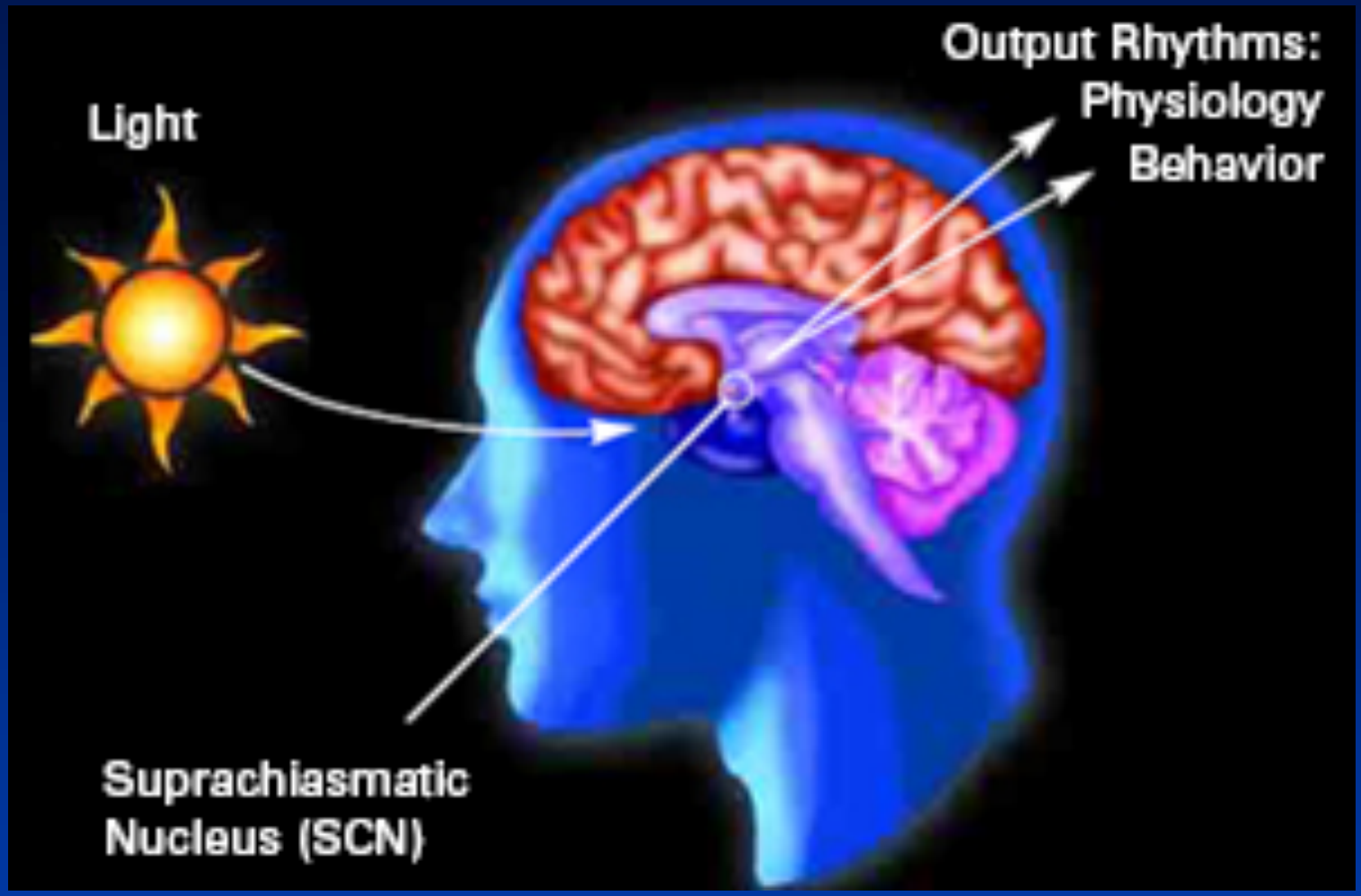
Other Negative Health Consequences of Shift Work

1. Immune dysfunction
    a) Autoimmune disorders, Infectious disease
2. Cardiovascular disease
    a) Hypertension, Heart attacks
3. Metabolic Disorders
    a) Type 2 Diabetes, Obesity, Fertility dysfunction
4. Mood Disorders
    a) Depression, Anxiety, Psychosis
5. Learning and memory

What are the Cellular Mechanisms underlying the Sleep/Wake Cycle?

1. How do we know what goes on outside?
   a) What does the eye “see”?
      i. Does the eye see objects or light?
   b) What does the brain see?
      i. What is the Suprachiasmatic Nucleus?
      ii. What does it do?

Suprachiasmatic Nucleus (SCN)



The SupraChiasmatic Nucleus (SCN): 'Big Ben' of the CNS

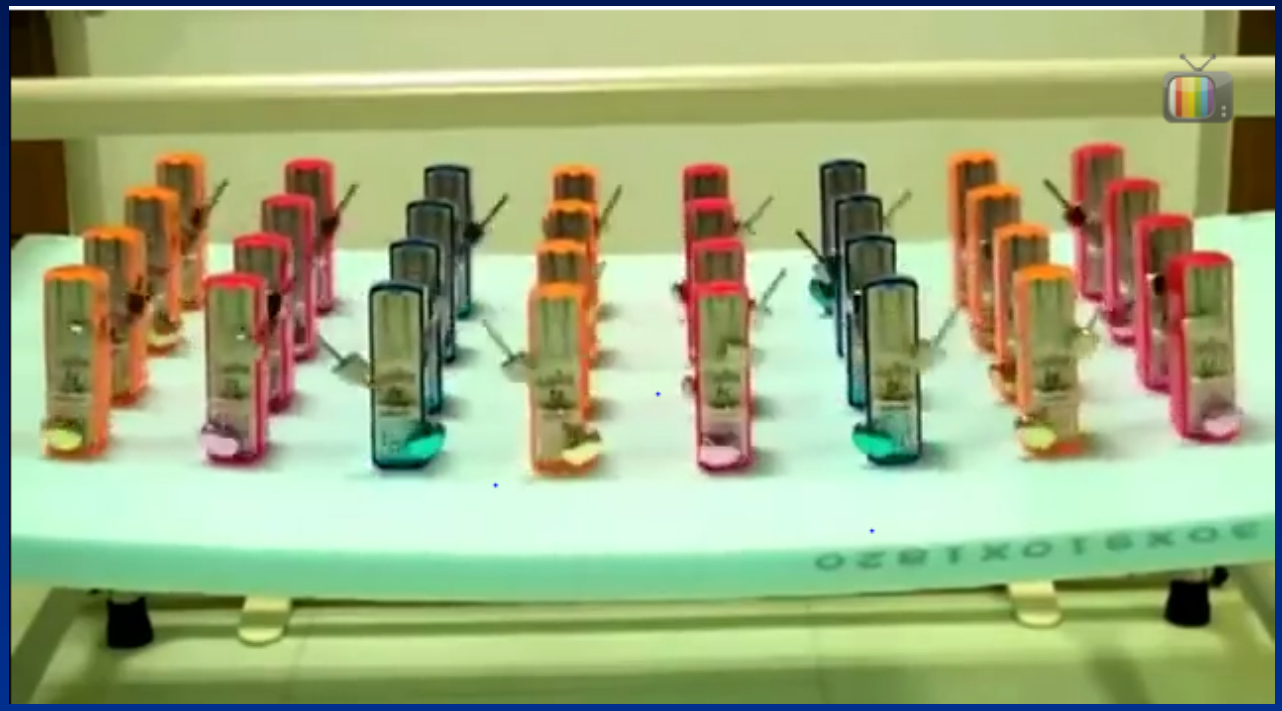
1. The body's clock
2. Where Melatonin works
3. Direct link to the retina
   a) Specific neurons transduce light only (not color or acuity)
4. Network of multiple oscillators
   a) coordinates daily rhythms in physiology and behavior
5. Synchronized by VIP responsive neurons
6. 'Jiggled' by GABA neurons
   a) Enables adaptation to changing seasons daylength
   b) But not able to adjust to abrupt changes like DST or jet lag
7. May be why hangover effects next morning

-G. Mark Freeman et al., GABA Networks Destabilize Genetic Oscillations in the Circadian Pacemaker, Neuron, 2013, DOI: 10.1016/j.neuron.2013.04.003

Sync metronomes

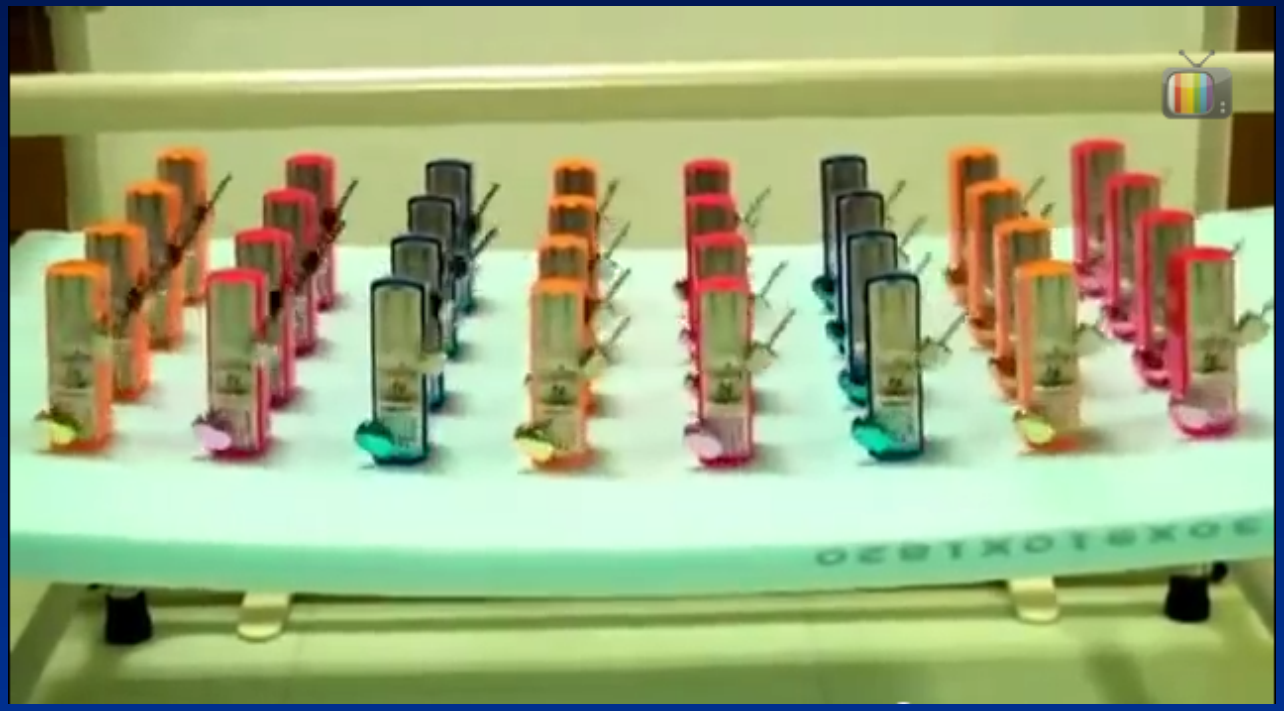
http://www.youtube.com/watch?feature=player_embedded&v=kqFc4wriBvE

Sync metronomes



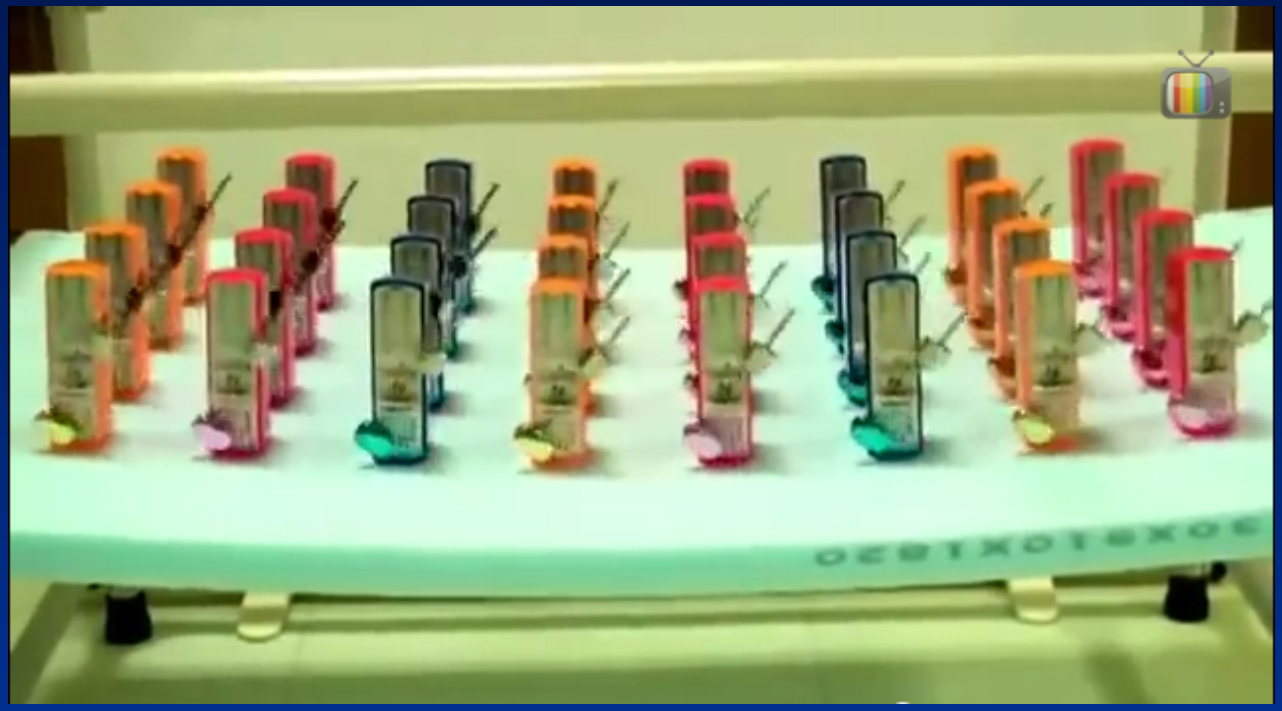
Metronomes asynchronous at this time point

Sync metronomes



Metronomes now synchronous at about 3:45’

Sync metronomes



If you “jiggle” the table, synchrony is lost - similar to purported role GABA system plays in SCN

Ok, I get the daylight effects, but are these rhythms really affected by the night?

1. Early western culture awareness that Full Moons were associated with “luna-tic” behavior
2. New data on full moon effects from laboratory recorded sleep

The Influence of the Moon on the Heads of Women-Anon 17th c.

Ok, I get the daylight effects, but are these rhythms really affected by the night?

The first reliable evidence that a lunar rhythm can modulate sleep structure in humans when measured under the highly controlled conditions of a circadian laboratory study protocol without time cues.

**Slow wave sleep (Deep Sleep) reduced by 30%*

http://www.cell.com/current-biology/retrieve/pii/S096098221300754 9

How can NO *ReNormalize* Our Circadian Rhythm?

1. Overwhelming evidence from field in general that Neurofeedback improves brain regulation = improved brain function
2. NO experience describes even more global and comprehensive improvement
   a) Suggests more stable, efficient cycling
      i. Leading to habitual pattern improvement
   b) Deep Brain Cleansing

More stable, efficient cycling

1. Presumption 1: brain is more responsive to neurohormones and neurotransmitters
   a) Operant conditioning enhances specific brain activity
2. Presumption 2: this effect results in improved sleep/wake cycles
   a) Evidence for this comes from clinical insomnia improvement reflects strong sleep/ wake cycles
   b) Evidence from anecdotal reports that awakening more refreshed, needing less sleep overall-needs to be tested

Operant Conditioning of Human EEG Spindles (*Not* what NO does!!)

1. Instrumental conditioning of hu-man sensorimotor rhythm (12-15 Hz, SMR; *note that visual reward was appearance of a "Sun"*)
   a) Physiological outcome: Increased amplitude and frequency of spindle activity
   b) Behavioral outcomes
      a) Improved declarative memory
      b) delayed sleep onset
2. SMR synchronization produces quiescence

Hoedlmoser K; Pecherstorfer T; Gruber G; Anderer P; Dop-pelmayr M; Klimesch W; Schabus M. Instrumental conditioning of hu-man sensorimotor rhythm (12-15 Hz) and its impact on sleep as well as declarative learning. *SLEEP* 2008;31(10):1401-1408.

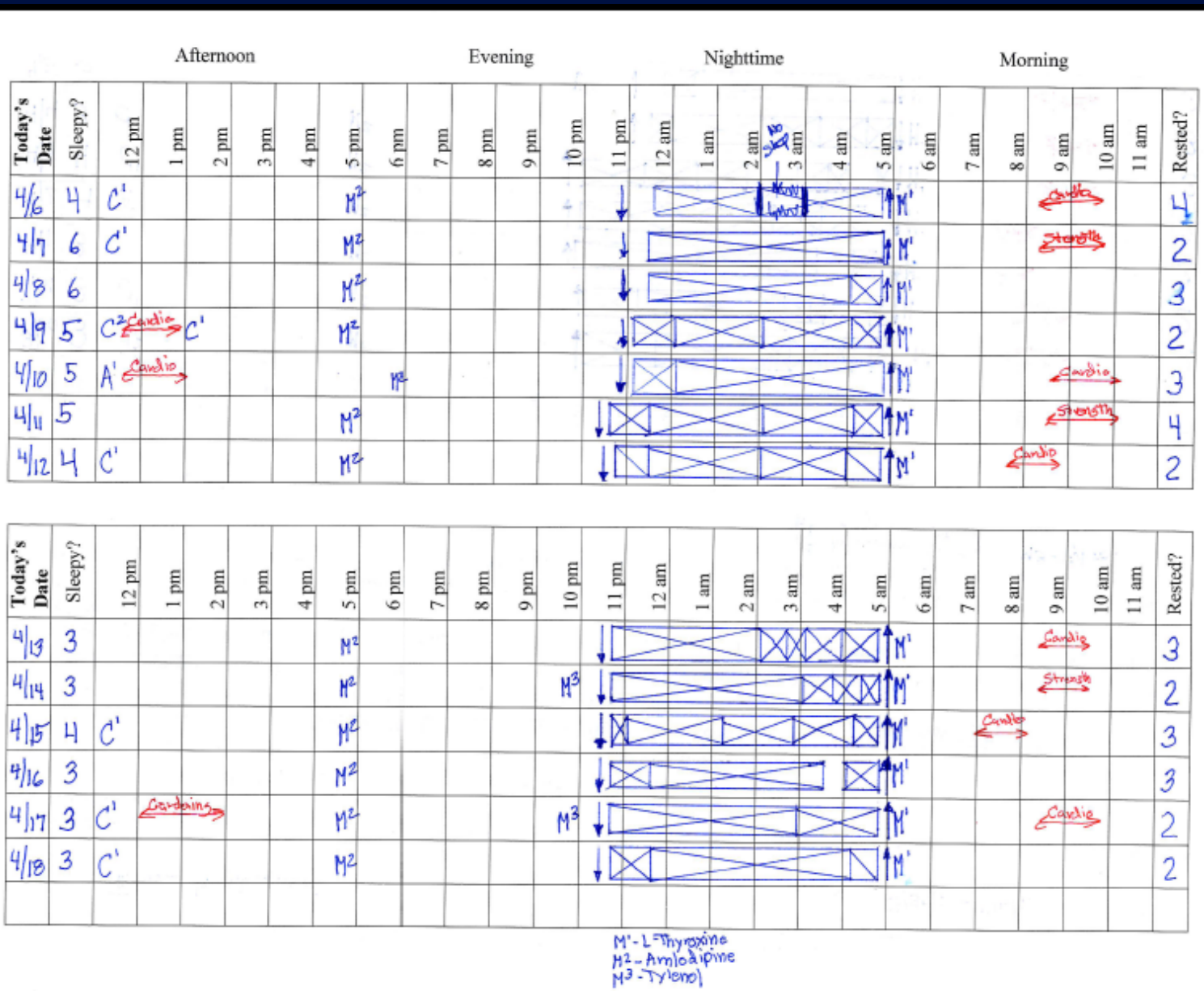
SLEEP HEALTHCARE of CT WEEKLY SLEEP & WAKE LOG

Name: _____ **Date:** 3/30/11 - 4/5/11

1. Take the time to fill out this form for last night's sleep when you get up to start your day. **(No need to watch the clock, just estimate sleep time or time awake).**
2. You will indicate **what time you actually began trying to fall asleep** by drawing a down arrow. ↓
3. You will indicate **what time you got up to start your day** with an up arrow. ↑
4. Shade the boxes showing **when you think you were sleeping**. example: 
5. If you are awake for more than half an hour, leave that area un-shaded.
6. **In the morning**, under the "rested" column, mark how rested you felt upon arising, on a scale of 1-7, **1** ***being most rested.***
7. **In the evening**, under the "sleepy" column, mark how sleepy you felt for most of the day, on a scale of 1-7, **7** ***being most sleepy***.
8. Before you go to bed indicate by **letter** what times you took (**M**)edication, (**C**)affeine (# of beverages or chocolate pieces), or (**A**)lcohol (# drinks, beers, or ounces), and shade in time for any naps that day (Note: use M1, M2 etc for different medications).

M2 - Amlodipine 5mg tab M3 - Tylenol
M1 - L-thyroxine .05 tab

		Afternoon					Evening					Nighttime									Morning						
Today's Date	Sleepy?	12 pm	1 pm	2 pm	3 pm	4 pm	5 pm	6 pm	7 pm	8 pm	9 pm	10 pm	11 pm	12 am	1 am	2 am	3 am	4 am	5 am	6 am	7 am	8 am	9 am	10 am	11 am	Rested?
3/30	3	C²					M²													M¹		Cardio Workout				2
3/31	3	C¹					M²													M¹		Strength Workout				2
4/1	3						M²													M¹		Cardio				2
4/2	4	A¹					M²													M¹		Cardio				2
4/3	4	C¹					M²													M¹			Cardio			3
4/4	3	C¹					M²													M¹			Strength			3
4/5	3											M²								M¹			Cardio			3


Afternoon
Evening
Nighttime
Morning
Today's Date
Sleepy?
12 pm
1 pm
2 pm
3 pm
4 pm
5 pm
6 pm
7 pm
8 pm
9 pm
10 pm
11 pm
12 am
1 am
2 am
3 am
4 am
5 am
6 am
7 am
8 am
9 am
10 am
11 am
Rested?
4/6 4 C' M² M' 4
4/7 6 C' M² M' 2
4/8 6 M² M' 3
4/9 5 C² Cardio C' M² M' 2
4/10 5 A' Cardio M² M' 3
4/11 5 M² M' 4
4/12 4 C' M² M' 2
4/13 3 M² M' 3
4/14 3 M² M³ M' 2
4/15 4 C' M² M' 3
4/16 3 M² M' 3
4/17 3 C' Curtains M² M³ M' 2
4/18 3 C' M² M' 2
M' - L-Thyroxine
M² - Amlodipine
M³ - Tylenol

Deep Cleansing

1. Presumption 1: During an NO session, brain operates much more efficiently by only responding to appropriate information, essentially screening out the superfluous, the false data
    a) Evidence from variety of anecdotal sources, Val data, including iSNR data I presented showing improved qEEGs
2. Presumption 2: this effect creates more metabolic waste needing to be cleared
    a) Evidence for this comes from sleep and learning data-when heavy academic load increased REM sleep

Sleep Drives Metabolite Clearance from the Adult Brain

Lulu Xie,[1*] Hongyi Kang,[1*] Qiwu Xu,[1] Michael J. Chen,[1] Yonghong Liao,[1] Meenakshisundaram Thiyagarajan,[1] John O'Donnell,[1] Daniel J. Christensen,[1] Charles Nicholson,[2] Jeffrey J. Iliff,[1] Takahiro Takano,[1] Rashid Deane,[1] Maiken Nedergaard[1]†

18 OCTOBER 2013 VOL 342 **SCIENCE** www.sciencemag.org

- A good night's sleep may be the key to preventing brain diseases such as Alzheimer's, a new study has found.
- Poor sleep may be linked to Alzheimer's
- Poor sleep tied to Alzheimer's-like brain changes

Self-reported Sleep and β-Amyloid Deposition in Community-Dwelling Older Adults Adam P. Spira, Alyssa A. Gamaldo, Yang An, Mark N. Wu, Eleanor M. Simonsick, Murat Bilgel, Yun Zhou, Dean F. Wong, Luigi Ferrucci and Susan M. Resnick.

- Shorter sleep duration and poorer sleep quality linked to Alzheimer's disease biomarker
- In Older Adults, Sleep Problems Tied to Alzheimer's

What about NO during sleep?

Is anything happening when we can't "hear" the interruptions?

What about NO *during* sleep?

1. Remember subliminal learning?
   a) Only worked for material presented during hypnagogic state
2. Remember what is supposed to happen during sleep?
   1. Rehearsing occurs during sleep which is why recall is better after an intervening sleep period
   2. Clearing out the metabolic waste improves next day function (Deep Cleansing)

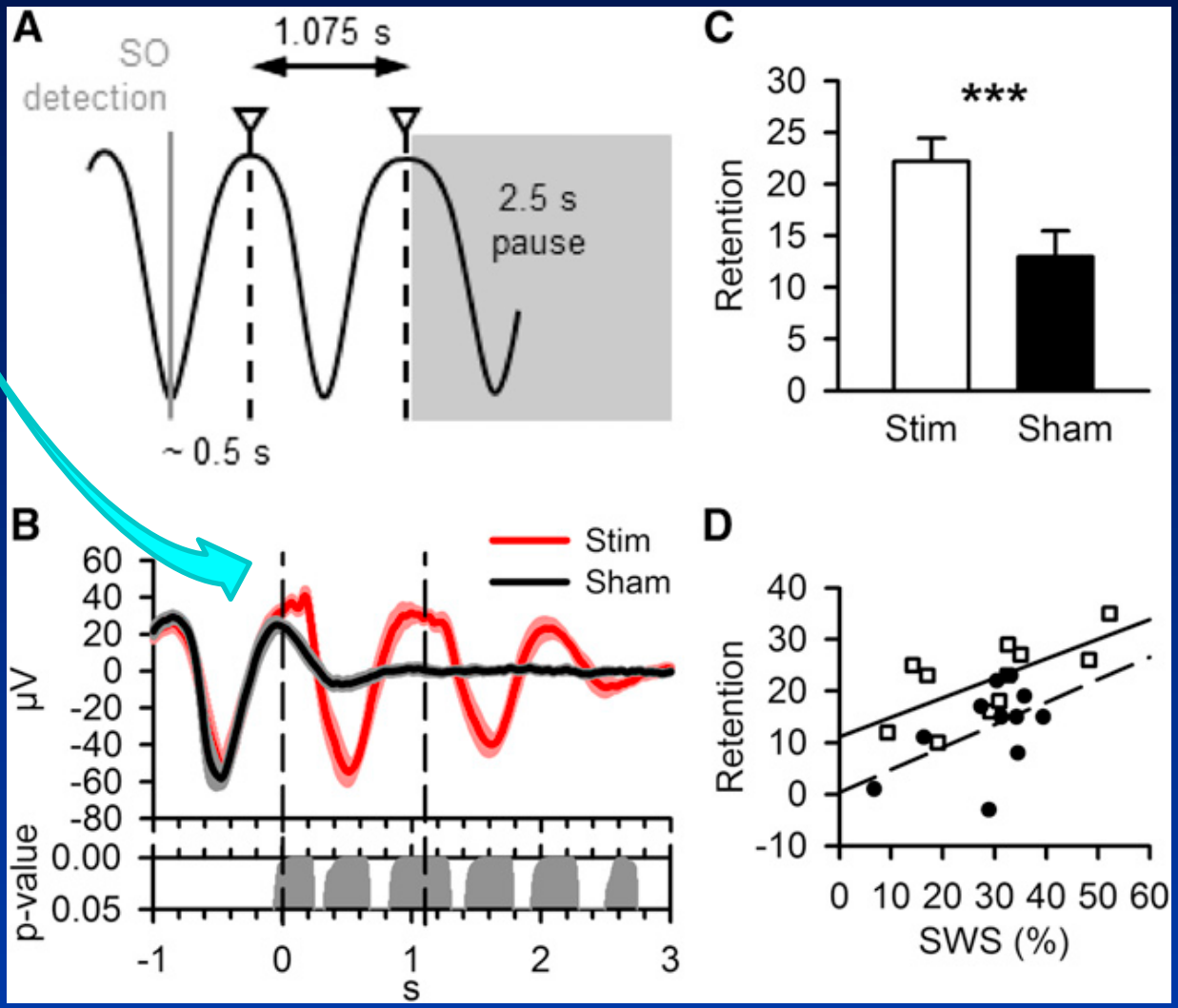
Recent Evidence for Exogenous "Information" Impacting Sleep

Ngo et al., Auditory Closed-Loop Stimulation of the Sleep Slow Oscillation Enhances Memory, Neuron (2013)

http://www.cell.com/neuron/retrieve/pii/S0896627313002304

- In-phase timed auditory stimulation enhanced spindle-driven slow wave oscillations in slow wave sleep (deep sleep)
- Increased overall amount of power in the slow wave freq band
- Resulted in significant improvement on memory task = positive functional outcome

Auditory Stimulation Increases Slow Wave Trains



And now the speculative part of the talk….

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2. Remember what is supposed to happen during sleep?
    1. Rehearsing occurs during sleep which is why recall is better after an intervening sleep period

And now the speculative part of the talk….

1. What about that *in between state* that occurs during sessions, you know when you go somewhere else…where/what is that?
   a) Is it a definable state of consciousness?
   b) Charles tart's mutual hypnosis paradigm

2. Open Discussion cause we really don't know… but as John Hurt says to Jodie Foster in the movie "Contact.."Wanna go for a ride?"

Thank You For Your Attention (*Your Enhanced Wake and Reduced Sleep Drives*)!