Insomnia

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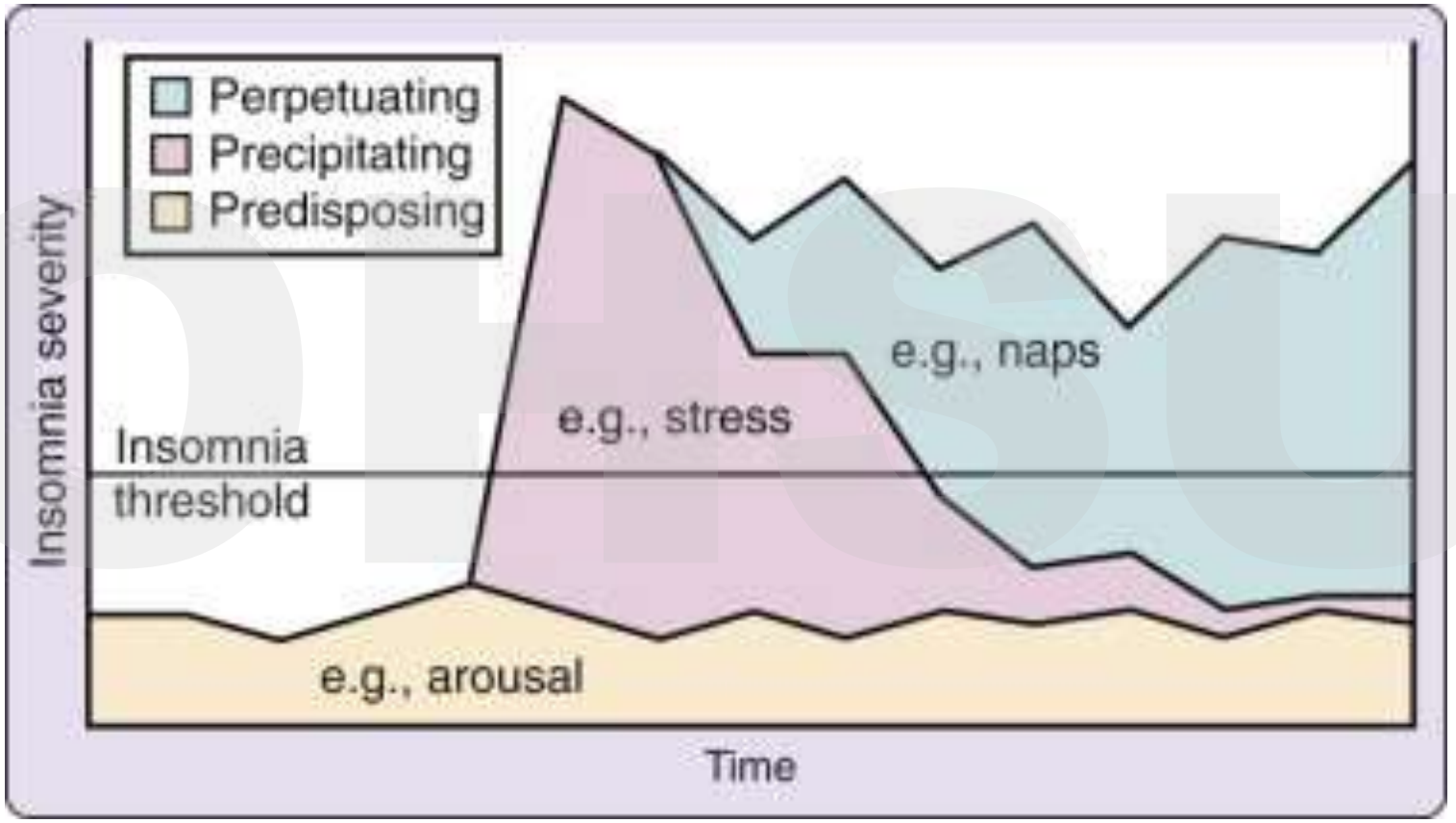
Insomnia

- Definitions
- Etiology
- Morbidity/Co-Morbidity
- Diagnosis
- Treatment
  - Pharmacologic
  - Behavioral
- Case

Definitions: DSM-V

- Insomnia Disorder (307.42)
- Dissatisfaction with the amount or quality of sleep along with:
  - Difficulty falling asleep
  - Difficulty staying asleep
  - Early-morning awakening
- "Causes clinically significant distress or impairment"
- Happens at least 3 nights per week
- Has lasted at least 3 months
- Not better or adequately explained by:
  - Inadequate opportunity for sleep
  - Another sleep disorder (e.g., sleep apnea, narcolepsy or a circadian rhythm sleep disorder)
  - Substance use
  - Other mental or medical disorders

Etiology



From: Kryger, Roth, Dement, eds., Principles and Practice of Sleep Medicine, 2011
Also see: Reimann et al. Sleep Med Rev 2010;14: 19-31

Etiology: Evidence for physiological hyperarousal

- Hyperarousal ← → Insomnia?
- Genetic component? Higher monozygotic twin concordance
- People with insomnia don't show evidence of sleep deprivation on multiple sleep latency test (MSLT, nap study)
- Increased high frequency EEG in non-REM sleep
- Increased metabolic rate (sleep & wake)
- Increased cortisol levels
- Increased sympathetic/decreased parasympathetic activity during sleep (HRV)

Reimann et al. Sleep Med Rev 2010;14: 19-31
Bonnet and Arand Sleep Med Rev 2010;14: 9-15

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Morbidity/Co-Morbidity

- Psychiatric: *prevalence* of any psychiatric disorder is 2-3x greater in insomniacs, depression *prevalence* is 4x greater
- Decreased quality of life
- Increased accidents and decreased productivity
- Increased *risk* of:
  - Hypertension
  - Diabetes
  - Metabolic syndrome (≥ 3: hyperglycemia, hypertriglyceridemia, increased waist circumference, HTN)
  - Myocardial infarction
  - Depression

Roth T, Journal of Clinical Sleep Medicine 2007; 3:S7-S10.
Vgontzas et al., Sleep 2009; 32: 491-497.
Vgontzas et al., Diabetes Care 2009; 32:1980-1985.
Troxel et al., Sleep 2010; 33: 1633-1640.
Laugsand et al., Circulation 2011; 124: 2073-2081
Laugsand et al., Euro Heart J 2013; 124: 2073-2081
Breslau N, Biol Psychiatry 1996;39:411-418
Chang PP, Am J Epidemiol 1997;146:105-114
Weissman MM, Gen Hosp Psych 1997;19:245-250

Morbidity/Co-Morbidity: Depression

Table 3. First onset of a psychiatric disorder over the subsequent year in individuals with insomnia and no psychiatric disorder as compared with individuals with neither

	At first interview			
	Insomnia and no psychiatric disorder	No insomnia and no psychiatric disorder		
Number at risk	414	4826	Odds ratio[a]	95% CI
First onset in following year	Rate/100			
Major depression	2.7	0.5	5.4*	2.6–11.3
Panic disorder	1.0	0.1	20.3*	4.4–93.8
Obsessive-compulsive disorder	1.6	0.7	2.2	0.9–5.1
Alcohol abuse	3.3	1.8	2.3*	1.2–4.3
Drug abuse	0.6	0.3	1.9	0.5–7.2

CI = confidence interval.

[a] Odds ratio adjusted by age, sex, and site.

* $p < 0.05$.

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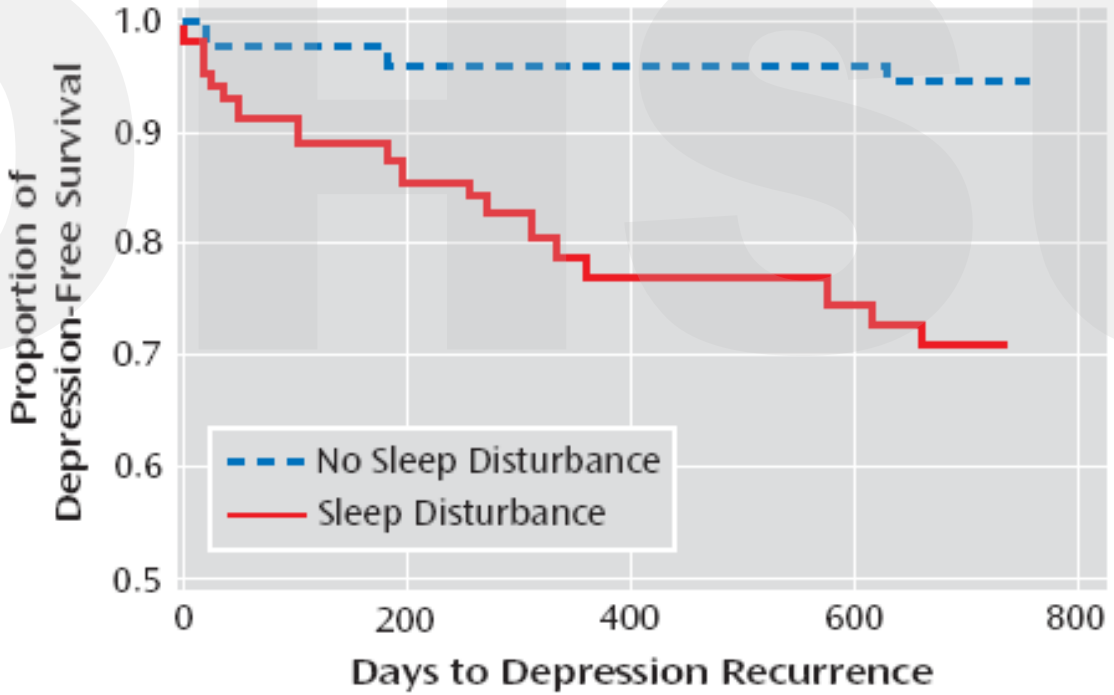
Morbidity/Co-Morbidity: Depression

FIGURE 1. Time to Depression for Older Adults With a Prior Depression History According to Sleep Disturbance at Baseline



Cho HJ, Am J Psych. 2008;165: 1543-1550.

Morbidity/Co-Morbidity: Hypertension

Table 2—Multivariable Adjusted Odds Ratio (95% CI) of Hypertension and Insomnia or Objective Sleep Duration

Sleep Difficulty	Model 1			Model 2			Model 3		
	Odds Ratio	95%	CI	Odds Ratio	95%	CI	Odds Ratio	95%	CI
Normal sleeping	1.00			1.00			1.00		
Poor sleep	1.30	0.98	1.72	1.25	0.94	1.70	1.23	0.92	1.65
Insomnia	2.76	1.82	4.20	2.55	1.66	3.90	2.41	1.57	3.70
Sleep duration									
> 6 h	1.00			1.00					
5-6 h	1.19	0.89	1.58	1.18	0.88	1.57	1.13	0.85	1.51
≤ 5 h	1.65	1.22	2.23	1.65	1.22	2.23	1.56	1.14	2.11

Model 1. Adjusted for age, race, sex, BMI, diabetes, and sampling weight.
Model 2. Adjusted for age, race, sex, BMI, diabetes, smoking status, alcohol consumption, depression, SDB, and sampling weight.
Model 3. Adjusted for age, race, sex, BMI, diabetes, smoking status, alcohol consumption, depression, SDB, and sampling weight and objective sleep duration (or insomnia). The interaction between insomnia and objective sleep duration is statistically significant, $P < 0.05$.

Measurements: *Insomnia* was defined by a complaint of insomnia with a duration ≥ 1 year, while *poor sleep* was defined as a complaint of difficulty falling asleep, staying asleep, or early final awakening.

Vgontzas et al., Sleep 2009; 32: 491-497.

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Morbidity/Co-Morbidity: Hypertension

Table 3—Multivariable Adjusted Odds Ratio (95% CI) of Hypertension Associated with Insomnia and Objective Sleep Duration

Sleep difficulty	Sleep duration	Sample size	Adjusted OR	95% CI	
				Low	Upper
Normal sleeping	> 6 h	527	1.00		
Poor sleep	> 6 h	249	0.79	0.52	1.20
Insomnia	> 6 h	86	1.31	0.70	2.46
Normal sleeping	5-6 h	235	0.86	0.60	1.22
Poor sleep	5-6 h	146	1.48	0.90	2.42
Insomnia	5-6 h	49	3.53	1.57	7.91
Normal sleeping	< 5 h	260	1.13	0.79	1.62
Poor sleep	< 5 h	125	2.43	1.36	4.33
Insomnia	< 5 h	64	5.12	2.22	11.79

All data adjusted for age, race, sex, BMI, diabetes, smoking status, alcohol consumption, depression, SDB, and sampling weight.
The interaction between insomnia and objective sleep duration is statistically significant, $P < 0.01$.
Compared to the common reference group, persons without insomnia/ poor sleep and slept more than 6 hours.

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Diagnosis

Diagnosis

- Made on the basis of diagnostic criteria
- Overnight sleep study only indicated for the diagnosis of *another sleep disorder* (e.g., sleep apnea or periodic limb movement disorder)
- What is useful? **History/ROS, questionnaires, sleep diaries** and wrist actigraphy
- Difficult in practice to differentiate between what were once called “primary” and “secondary” insomnias

Diagnosis

- History of the Insomnia
  - When did it begin?
  - Any known precipitants?
  - Usual questions:
    - Timing (number of episodes & frequency)
    - Duration
    - Severity (e.g., ISI questionnaire),
    - Any known modifying factors (e.g., stress or pain)?

Diagnosis

Insomnia Severity Index

The Insomnia Severity Index has seven questions. The seven answers are added up to get a total score. When you have your total score, look at the 'Guidelines for Scoring/Interpretation' below to see where your sleep difficulty fits.

For each question, please CIRCLE the number that best describes your answer.

Please rate the CURRENT (i.e. LAST 2 WEEKS) SEVERITY of your insomnia problem(s).

Insomnia Problem	None	Mild	Moderate	Severe	Very Severe
1. Difficulty falling asleep	0	1	2	3	4
2. Difficulty staying asleep	0	1	2	3	4
3. Problems waking up too early	0	1	2	3	4

4. How SATISFIED/DISSATISFIED are you with your CURRENT sleep pattern?

Very Satisfied	Satisfied	Moderately Satisfied	Dissatisfied	Very Dissatisfied
0	1	2	3	4

5. How NOTICEABLE to others do you think your sleep problem is in terms of impairing the quality of your life?

Not at all Noticeable	A Little	Somewhat	Much	Very Much Noticeable
0	1	2	3	4

6. How WORRIED/DISTRESSED are you about your current sleep problem?

Not at all Worried	A Little	Somewhat	Much	Very Much Worried
0	1	2	3	4

7. To what extent do you consider your sleep problem to INTERFERE with your daily functioning (e.g. daytime fatigue, mood, ability to function at work/daily chores, concentration, memory, mood, etc.) CURRENTLY?

Not at all Interfering	A Little	Somewhat	Much	Very Much Interfering
0	1	2	3	4

Guidelines for Scoring/Interpretation:

Add the scores for all seven items (questions 1 + 2 + 3 + 4 + 5 +6 + 7) = _____ your total score

Total score categories:
0–7 = No clinically significant insomnia
8–14 = Subthreshold insomnia
15–21 = Clinical insomnia (moderate severity)
22–28 = Clinical insomnia (severe)

Used via courtesy of www.myhealth.va.gov with permission from Charles M. Morin, Ph.D., Université Laval

Diagnosis

- Characterizing the Insomnia
  - Routine prior to trying to go to sleep
  - **Range** of bedtimes and wake times (including days off)
  - Bedtime routine (e.g., lights out right away?)
  - How long does it take to fall asleep, number & duration of awakenings, duration of sleep, duration of time in bed
    - Sleep latency
    - Wake after sleep onset (WASO)
    - Total Sleep Time (TST)
    - Sleep Efficiency (SE) = percentage of sleep opportunity that is sleep
  - What do they do when awake (e.g., stay in bed?)

Diagnosis

- Characterizing the Insomnia (cont.)
  - Excessive mental activity? Worry or sadness (even if they don't meet GAD or MDD criteria)?
  - Worry about sleep itself? Excessive efforts to fall asleep?
  - Any problems with noise, temperature, light or safety?
  - Does pain or tinnitus disturb sleep?
  - Do they nap? Can they nap? Do they try to catch up on sleep after a bad night?
  - Do they ever sleep well (e.g., away from their usual environment)?

Diagnosis

- Sleep ROS:
  - Snoring, witnessed apneas, choking/gasping, reflux, nocturia, morning headaches, morning dry mouth, daytime somnolence, or napping? - Sleep Apnea
  - Nightmares? Dream enactment? – PTSD vs trauma associated sleep disorder vs REM Behavior disorder
  - Bruxism?
  - Sleepwalking or sleep talking? - Slow-wave sleep parasomnias
  - *"Do you have a restless, nervous, tingly, or creepy-crawly feeling in your legs that disrupts your ability to fall or stay asleep?"* - Restless Legs Syndrome
  - Kicking or twitching during sleep? - Periodic Limb Movement Disorder
  - Sleep paralysis, hypnogognic/hypnopomic hallucinations, cataplexy, & daytime somnolence? - Narcolepsy

Diagnosis

- The history or characterization of insomnia as well as the sleep ROS may seem obvious
- However, they impact treatment even if there isn’t complete diagnostic clarity

Treatment

Treatment

- Treat underlying Medical or Psychiatric Condition (insomnia symptoms can remain)
- Improve sleep hygiene (limited data on efficacy)
- Change environment
- Cognitive-Behavioral Therapy for Insomnia (CBT-I)
- Pharmacologic
- Light and melatonin (“chronotherapy”)

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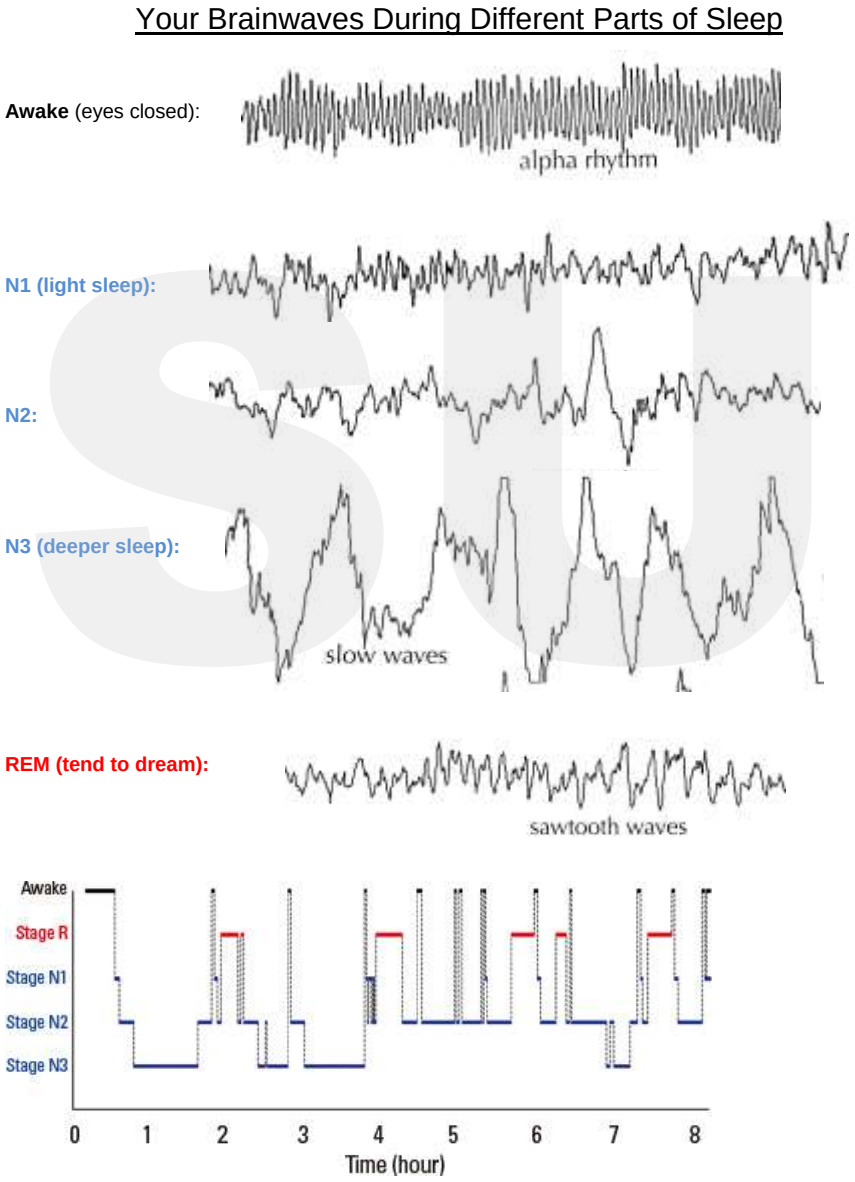
Treatment: Patient Education

Treatment: Patient Education

- Sleep is a dynamic & active process
- Different parts (stages) of sleep based on the EEG
- The concept of local sleep

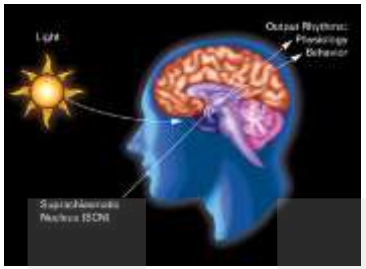


Vyazovsky et al., Nature 2011; 472: 443-447
Nobili et al., Prog Brain Res 2012; 199: 219-232

Treatment: Patient Education

- There are multiple areas in the brain involved in generating sleep & wakefulness
- The “two-process” model of sleep: the 24-hour body clock and homeostatic sleep drive

24-Hour Body Clock



From: http://www.nigms.nih.gov/Education/Pages/Factsheet_CircadianRhythms.aspx

There is a clock in your brain (20,000 nerve cells). The Clock is reset by light through the eyes. It tells your body what time it is. It tries to wake you up when it thinks it is daytime and it tries to make you sleepy when it thinks it is nighttime.

Sleep Drive

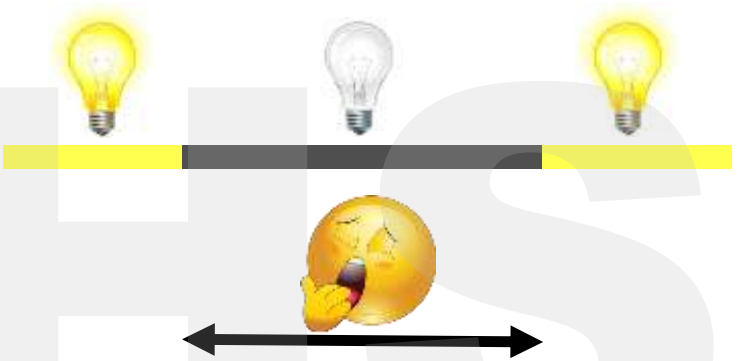
You build up more sleep drive the longer you are awake. You have less sleep drive the longer you are asleep. You can think of it like the gas that powers a car: you “fuel up” during the day by building up sleep drive and you “burn up” sleep drive when you sleep.

Treatment: Patient Education

What is Jet Lag?

(or)

Why light is important for sleep



Portland, OR:

20 22 **00** 02 04 06 **08** 10 12

New York, NY:

23 01 **03** 05 07 09 **11** 13 15

Treatment: Patient Education

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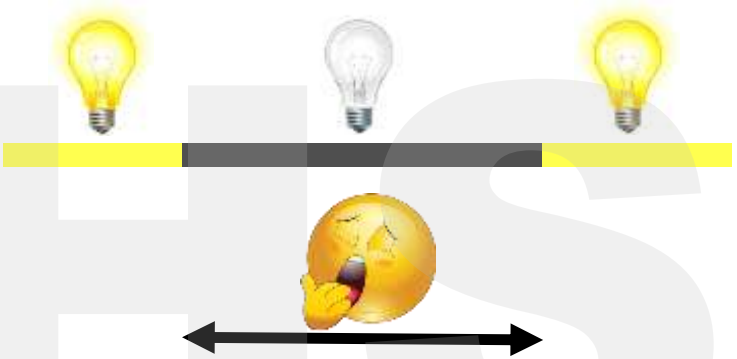


Portland, OR:

20 22 **00** 02 04 06 **08** 10 12

Shifts to and from Daylight Saving Time and Incidence of Myocardial Infarction

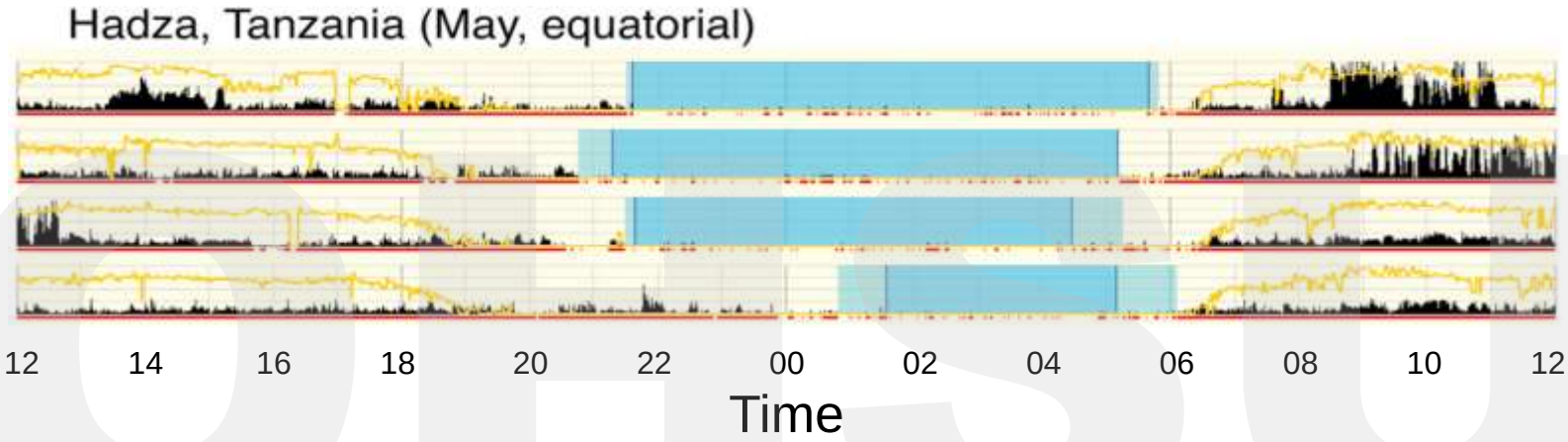
N ENGL J MED 359;18 WWW.NEJM.ORG OCTOBER 30, 2008

New York, NY:

23 01 **03** 05 07 09 **11** 13 15

Treatment: Patient Education

Sleep in hunter-gatherers

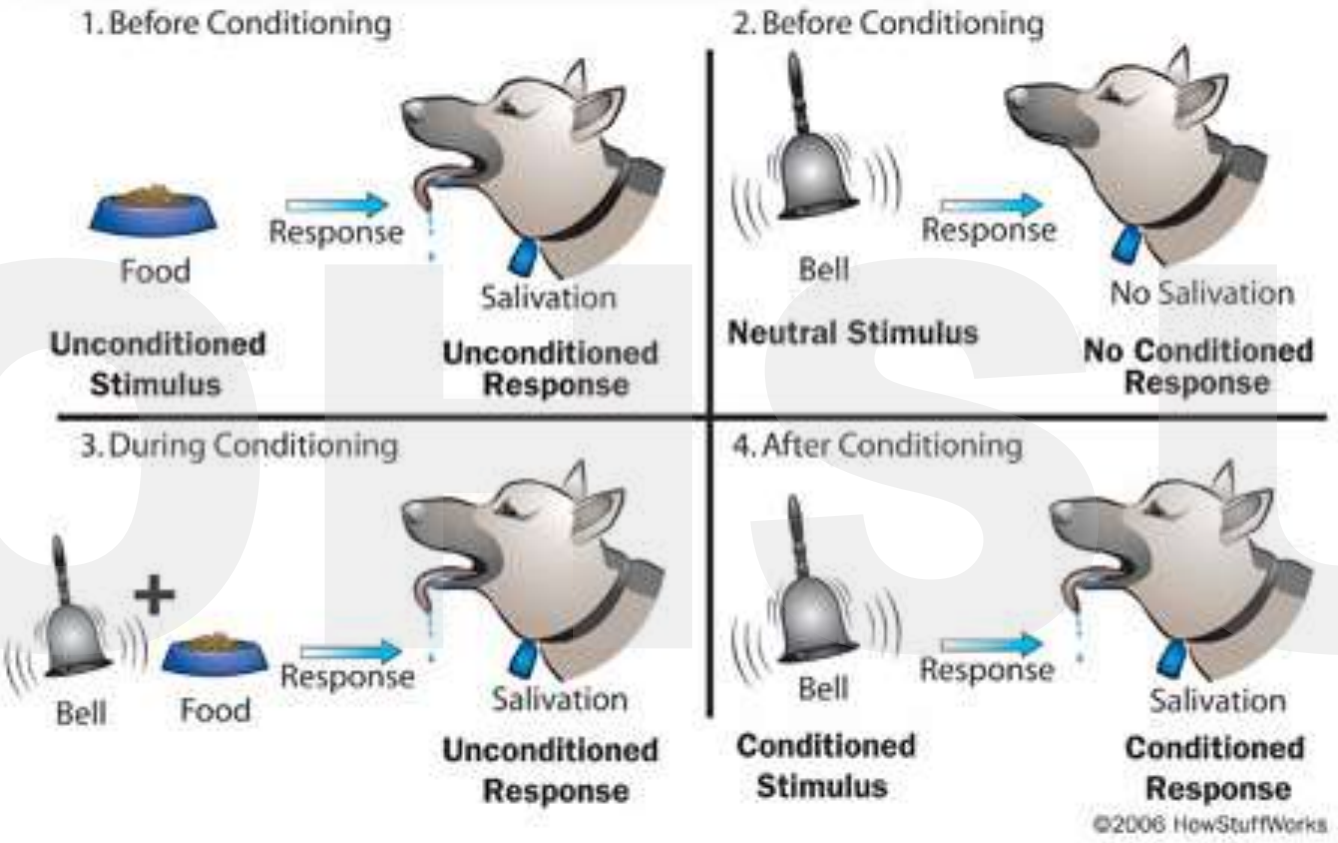


Black = when they were moving
Red = awake
Yellow = light level
Dark Blue = main sleep period

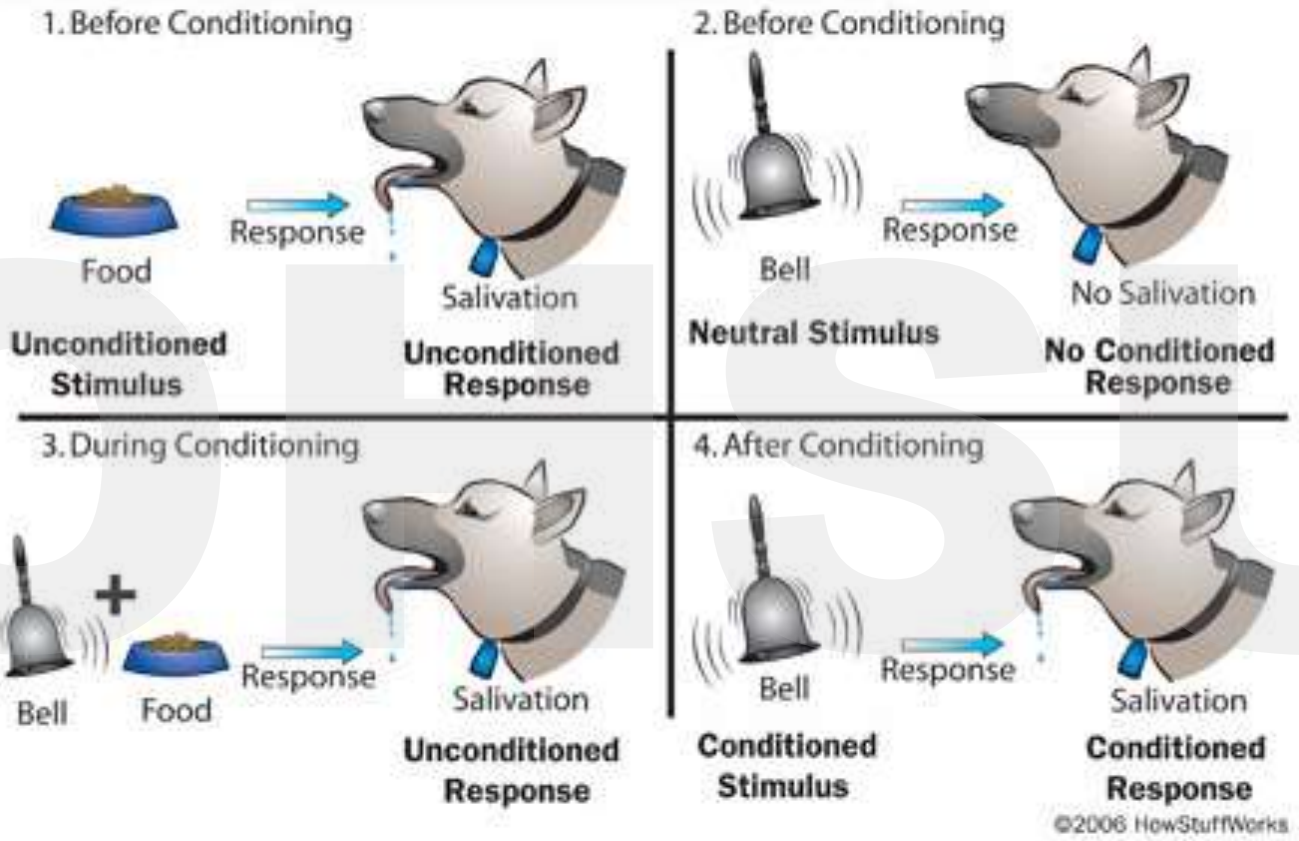
Yetish et al., Curr Biol. 2015;25: 1-7

- Sleep under “natural” light/dark conditions
- Cultural ideas about sleep

Treatment: Patient Education



Treatment: Patient Education

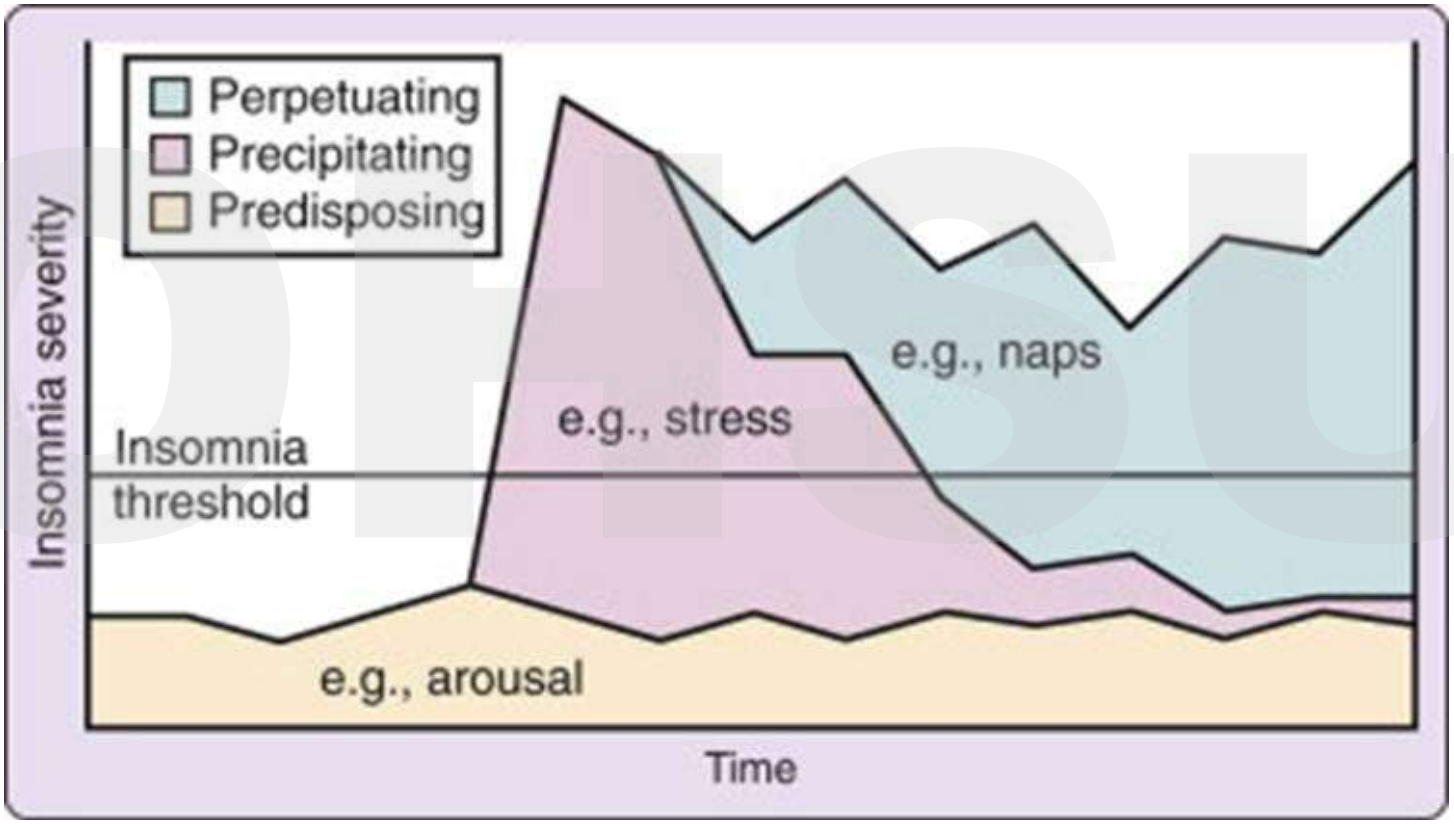


Resetting of the circadian clock by a conditioned stimulus

Shimon Amir & Jane Stewart

NATURE · VOL 379 · 8 FEBRUARY 1996

Treatment: Patient Education



From: Kryger, Roth, Dement, eds., Principles and Practice of Sleep Medicine, 2011

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Treatment: Pharmacologic

Table 3. Medications Commonly Used for Insomnia.

Medication	Dose in Adults		Half-Life	Most Common Side Effects
	<65 yr of age	≥65 yr of age		
Antihistamines	*mg*		*hr*	
Benzodiazepine-receptor agonists				Daytime sedation, ataxia, anterograde amnesia, complex sleep-related behaviors (e.g., sleepwalking)
Temazepam (Restoril)*	7.5–30	7.5–15	8–10	
Lorazepam (Ativan)	0.5–2	0.5–1	8–12	
Eszopiclone (Lunesta)*	2–3	1–2	6–9	Unpleasant taste†
Zolpidem (Ambien)*	5–10	2.5–5	2.5	
Triazolam (Halcion)*	0.125–0.5	0.125–0.25	2.5	
Zaleplon (Sonata)*	5–20	5–10	1	
Antidepressants				
Trazodone (Desyrel)	25–100	25–100	6–8	Daytime sedation, orthostasis
Mirtazapine (Remeron)	7.5–30	7.5–30	20–30	Daytime sedation, anticholinergic effects, weight gain
Doxepin (Sinequan, Silenor)*	10–50 (3–6 approved)	10–50	12–18	Daytime sedation, anticholinergic effects, weight gain (not at approved doses)
Orexin antagonist: suvorexant (Belsomra)*	10–20	10–20	9–13	Daytime sedation
Melatonin agonist: ramelteon (Rozerem)*	8	8	1	Daytime sedation
Anticonvulsant: gabapentin (Neurontin)	100–900	100–900	5–9	Daytime sedation, dizziness, weight gain

Winkleman NEJM 2015;373:1437-1444

More detailed review: Buysee JAMA 2013;309: 706-716

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Treatment

- Treat underlying Medical or Psychiatric Condition (insomnia symptoms can remain)
- Improve sleep hygiene (limited data on efficacy)
- Change environment
- Cognitive-Behavioral Therapy for Insomnia (CBT-I)
- Pharmacologic
- Light and melatonin (“chronotherapy”)

Treatment: Behavioral

- Progressive relaxation
- EMG biofeedback
- Guided imagery
- Stimulus control therapy: in bed only when sleepy, bed/bedroom is for sleep and sex only, & get out of bed when unable to sleep
- Bed Restriction: fixed waketime, change bedtime by 15 minutes if sleep efficiency >90% in the last week
- Regular sleep schedule and light/dark schedule
- Requires the use of a sleep diary

Morin CM, et al. Sleep 2006;29:1398-1414

Treatment: Behavioral

- Progressive relaxation
- EMG biofeedback
- Guided imagery
- Stimulus control therapy: in bed only when sleepy, bed/bedroom is for sleep and sex only, & get out of bed when unable to sleep
- Bed Restriction: fixed waketime, change bedtime by 15 minutes if sleep efficiency >90% in the last week
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- Requires the use of a sleep diary

Morin CM, et al. Sleep 2006;29:1398-1414

Treatment: Behavioral

Table 1. Cognitive-Behavioral Interventions for Insomnia[a]

Intervention	General Description	Specific Techniques
Sleep hygiene education	Recommendations promoting behaviors that help sleep, discouraging behaviors that interfere with sleep	Do not try to sleep. Avoid stimulants (caffeine, nicotine). Limit alcohol intake. Maintain a regular sleep schedule 7 nights per wk. Avoid naps. Get regular exercise at least 6 h prior to sleep. Keep the bedroom dark and quiet.
Stimulus control	Based on operant and classical conditioning principles: nonsleep activities and the bedroom environment can serve as stimuli that interfere with sleep. Treatment prescribes behaviors that strengthen associations between the environment and sleep.	Go to bed only when sleepy. Use the bed and bedroom for sleep only. Do not read, watch television, talk on the phone, worry, or plan activities in the bedroom. If unable to fall asleep within 10-20 min, leave the bed and the bedroom. Return only when feeling sleepy again. Set the alarm and wake up at a regular time every day. Do not use the snooze button on the alarm. Do not nap during the day.
Sleep restriction therapy	Based on experimental evidence that sleep is regulated by circadian and homeostatic processes. Treatment increases homeostatic sleep drive by reducing time in bed and maintaining a consistent wake time in the morning to reinforce circadian rhythms.	Restrict time awake in bed by setting strict bedtime and rising schedules limited to the average number of hours of actual sleep reported in 1 night. Keep a fixed wake-up time, regardless of actual sleep duration. If after 10 d sleep efficiency is lower that 85%, further restrict bedtime by 15-30 min. Increase time in bed by advancing bedtime by 15-30 min when the time spent asleep is ≥85% of time in bed.

Buysee JAMA 2013;309: 706-716

Treatment: Behavioral

Bed Restriction

1. Keep a sleep diary throughout the treatment period.
2. First work on keeping the same **lights out & lights on schedule**. Keep the same bedtimes and out-of-bed times on weekends and weekdays. Get help from family or friends in getting out of bed at the same time each day.
3. If you start with 6 hours of bed restriction, determine your starting "lights out" time by subtracting 6 hours from your chosen wake time.
4. If you are able to obtain good sleep (that is, about 90% of the time you are in bed is sleep) for three days, add on 15 minutes of time in bed. Add on the additional time in bed at the beginning of the night, keeping your wake time the same.
5. Every three days reevaluate: if you are obtaining good sleep add on another 15 minutes of time in bed. If insomnia returns, subtract 15 minutes of time in bed.
6. Make sure you get as much rest as you need during your wake/lights on time.

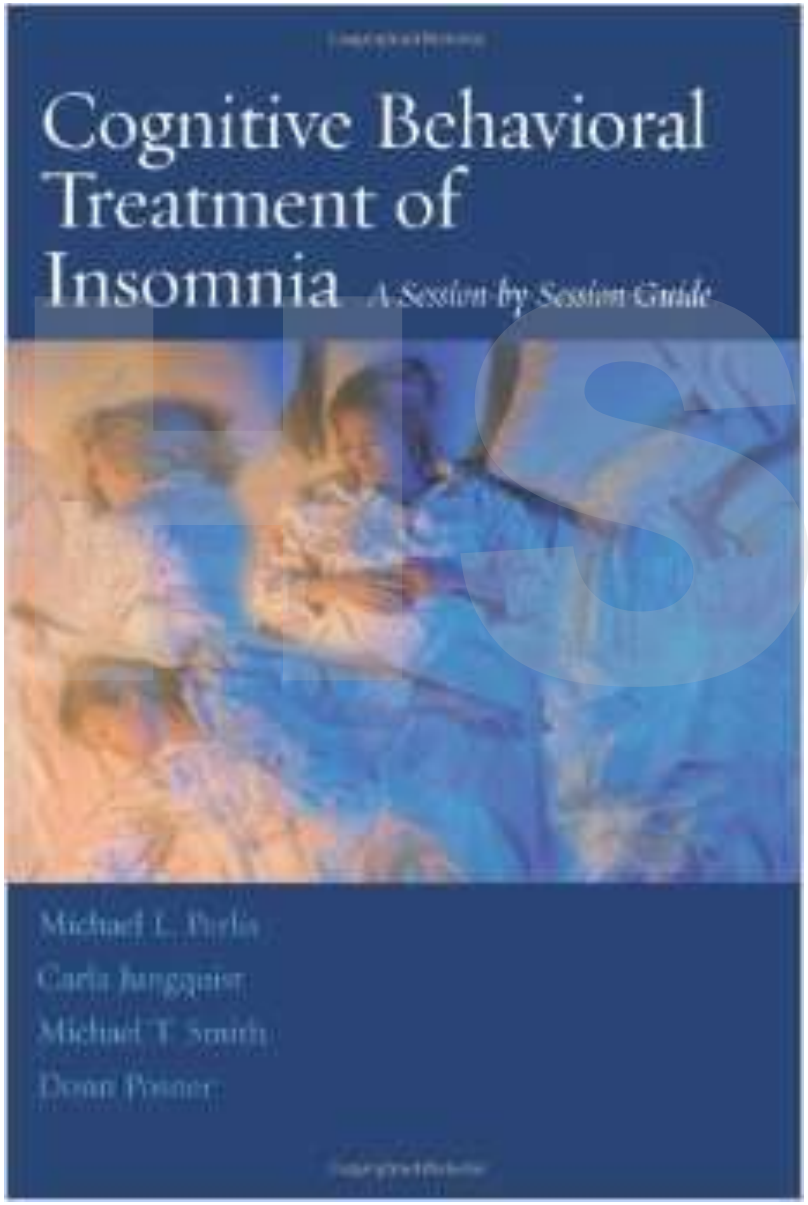
Starting Lights out/In Bed: _____

Lights On/Out of Bed: _____

Stimulus Control

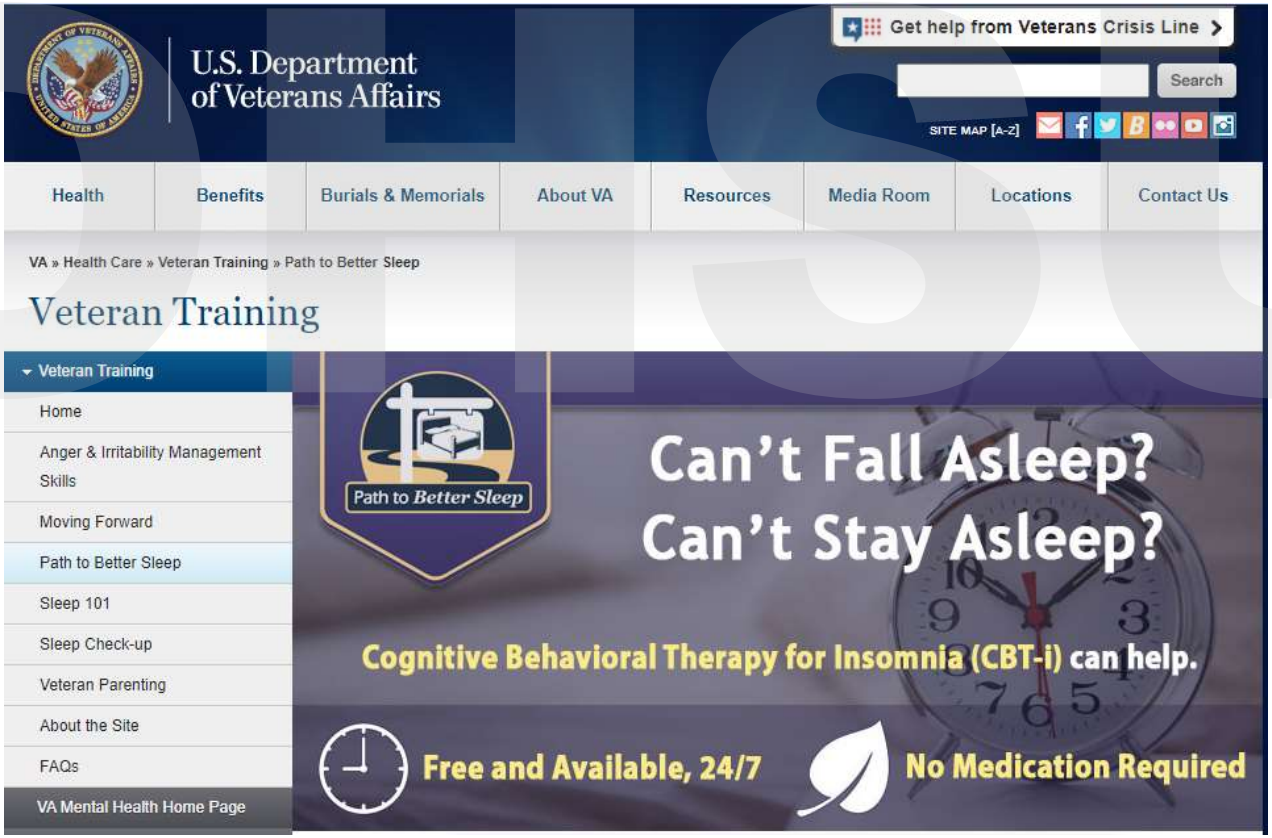
1. The goal of stimulus control is to have your brain think the bed is a place to sleep instead of a place to be awake.
2. **The bed is for sleep and sex only**. Go to bed only when you are sleepy.
3. If you don't fall asleep in 15 to 20 minutes, get up, go into another room (if possible), and **lay quietly in darkness** until sleepy. This other place is your "insomnia bed." Try listening to music, a book on tape, or the radio.
4. Don't watch the clock. Just guess when 15-20 minutes have passed. Plan ahead of time what you are going to do during the time you are out of bed.

Treatment: Behavioral



Treatment: Behavioral

Free online CBT-I:
https://www.veterantraining.va.gov/insomnia/



Treatment: Efficacy (Pharmacologic & Behavioral)

Variable	Average Improvement (consider study length and how measured – PSG vs. diary)
Sleep Latency	~15 to 30 minutes faster
Number of Awakenings	~ one less awakening
Total Sleep Time	~20-60+ minutes more sleep

Smith MT et al., Am J Psych. 2002;159:5-11
Buysee JAMA 2013;309: 706-716
Krystal AD et al., Sleep. 2008;31:79-90.
Glass et al. J Clin Psychopharm 2008; 28: 182-188
Krystal, et al. Sleep 2010; 33:1553-61
Michelson et al. Lancet Neurol 2014; 13: 461-471
Morin CM, et al. JAMA 1999;281:991-9
Jacobs GD, et al. Arch Intern Med 2004;164:1888-1896

Treatment: Comparisons

- Similar efficacy pharmocologic vs. cognitive-behavioral treatments in several studies
- 8 weeks of CBT vs. temazepam vs. combined treatment.

Morin CM, et al. JAMA 1999;281:991-9
Jacobs GD, et al. Arch Intern Med 2004;164:1888-1896
Morin CM, et al. Sleep 2006;29:1398-1414

Treatment: Comparisons

- 8 weeks of: temazepam (7.5-30 mg, avg=20 mg), placebo, CBT-I (8x90 min.), or combination.
- Temazepam increased total sleep time by 43.7 min.
- CBT-I increased total sleep time by 30.5 min. and by 65.2 min. at 2 years
- Combo increased total sleep time by 42.2 min.
- Placebo increased total sleep time by 19.7 min.

Table 2. Group Means and Number of Subjects in Each Treatment Condition*

Assessment Modes	CBT	PCT	Combined	Placebo
		Total Sleep Time		
Sleep diary				
Pretreatment	321.50 (79.8)	340.21 (73.6)	289.77 (64.7)	331.04 (59.5)
Posttreatment	352.00 (52.4)	383.90 (56.8)	331.93 (65.4)	350.70 (64.7)
3-mo Follow-up	355.57 (54.34)	373.53 (73.6)	327.75 (87.4)	370.34 (75.3)
12-mo Follow-up	375.32 (54.07)	353.52 (61.8)	317.04 (98.0)	319.75 (80.0)
24-mo Follow-up	386.70 (63.41)	351.73 (60.1)	330.63 (85.6)	330.53 (116.0)
Polysomnography				
Pretreatment	353.90 (43.8)	342.90 (51.0)	346.90 (45.8)	371.00 (50.1)
Posttreatment	360.70 (34.4)	378.20 (46.3)	356.10 (38.0)	373.80 (49.5)

*CBT indicates cognitive-behavior therapy; PCT, pharmacotherapy. All data are mean (SD). Numbers following parentheses are number of subjects in the group.

Morin CM, et al. JAMA 1999;281:991-9

Treatment: Comparisons

TABLE 2. Efficacy of Pharmacotherapy Compared With Behavioral Therapy in 21 Studies of Persistent Insomnia

Subjective Sleep Outcome Measure (Based on Sleep Diary)	Pretreatment Value		Posttreatment Value		Difference Between Pretreatment and Posttreatment Means		Number of Studies	Number of Subjects	Weighted Effect Size[a]		95% CI for Difference Between Effect Sizes
	Mean	SD	Mean	SD	Value	%			Mean	SD	
Sleep latency (minutes)											0.17 to 1.04
Pharmacotherapy	48.85	29.73	34.36	26.26	–14.49	29.7	6	129	0.45	0.28	
Behavioral therapy	54.24	28.52	30.93	16.03	–23.31	43.0	12	225	1.05[b]	0.76	
Number of awakenings											–1.24 to 1.5
Pharmacotherapy	3.00	1.99	1.83	1.37	–1.17	39.0	4	108	0.97	1.00	
Behavioral therapy	2.44	1.84	1.67	1.59	–0.77	31.6	4	58	0.83	1.30	
Wake time after sleep onset (minutes)											—[c]
Pharmacotherapy	55.09	37.80	29.49	19.50	–25.60	46.5	1	17	0.89	0.29	
Behavioral therapy	68.60	40.27	30.22	23.98	–38.38	55.9	5	81	1.03	0.19	
Total sleep time (minutes)											–0.25 to 1.01
Pharmacotherapy	332.08	55.32	372.59	48.97	40.51	12.2	6	130	0.84	0.76	
Behavioral therapy	333.28	63.66	352.89	44.22	19.61	5.9	8	146	0.46	0.62	
Sleep quality rating[d]											–1.70 to 1.22
Pharmacotherapy	3.10	0.64	3.73	0.93	0.63	20.3	4	109	1.20	1.30	
Behavioral therapy	3.38	0.66	4.34	1.30	0.96	28.4	5	82	1.44	1.20	

[a] Overall weighted effect size calculated by the formula (Σ[di*N]/Σ[N]), where *di* is the effect size of the individual study.
[b] Behavioral therapy showed greater reductions in sleep latency than pharmacotherapy (t=2.88, df=20.62, p=0.01, unequal variance).
[c] Confidence interval was not calculated because there was only one pharmacological study that included wake time after sleep onset.
[d] Sleep quality ratings were standardized across studies so that higher scores reflect better sleep quality.

Smith MT et al., Am J Psych. 2002;159:5-11.

Treatment: Comparisons

TABLE 2. Efficacy of Pharmacotherapy Compared With Behavioral Therapy in 21 Studies of Persistent Insomnia

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[d] Sleep quality ratings were standardized across studies so that higher scores reflect better sleep quality.

Smith MT et al., Am J Psych. 2002;159:5-11.

Treatment: Reviews

Table 2. Quantitative Reviews of Treatment Efficacy in Chronic Insomnia[a]

Source	Studies Reviewed	Major Findings
Psychological and behavioral treatments		
Morin et al,[9] 1994	59 Controlled studies of psychological-behavioral treatments (n = 2102)	Moderate to large effect sizes (d = 0.42-0.88) for short-term outcomes of sleep latency, wake after sleep onset, number of awakenings, total sleep time Effects sizes maintained at follow-up
Murtagh et al,[7] 1995	66 Outcome studies (n = 1907)	Moderate to large effect sizes (d = 0.49-0.94) for short-term outcomes of sleep latency, total sleep time, number of awakenings, sleep quality Effects maintained at long-term follow-up
Pallesen et al,[8] 1998	13 Studies Participants with minimum age 50 y and group mean age >60 y (n = 388)	Small to moderate effect sizes (d = 0.15-0.61) for posttreatment outcomes of sleep latency, wake after sleep onset, number of awakenings, total sleep time Moderate effect sizes (0.37-0.66) for long-term outcomes
Smith et al,[10] 2002	21 Studies 6 Pharmacologic RCTs (n = 220 participants) 14 Behavioral RCTs (n = 250)	Moderate to large effect sizes (d = 0.46-1.44) for outcomes of sleep latency, wake after sleep onset, total sleep time, sleep quality Effect size for sleep latency was larger in behavioral than pharmacologic treatment studies
Irwin et al,[11] 2006	23 RCTs of behavioral treatments for chronic insomnia Younger and older adult samples	Small effect sizes for total sleep time Moderate to large effect sizes (0.50-0.79) for sleep quality, latency, efficiency, wake after sleep onset Equivalent effects in younger and older adults except for total sleep time (smaller effect size in older adults)
Montgomery et al,[12] 2009	6 RCTs of CBT-I Adults aged >60 y with primary insomnia (n = 324)	Significant mean differences pre-post treatment for wake after sleep onset (self-report and polysomnography), sleep efficiency (polysomnography) Mean differences not statistically significant for sleep latency, total sleep time (self-report and polysomnography), sleep efficiency (self-report)
Van Straten et al,[13] 2009	10 Controlled trials of self-help interventions (eg, books, Internet, audiotapes) vs controls and in-person treatment (n = 1000)	Effect sizes small to moderate (d = 0.02-0.44) for total sleep time, sleep efficiency, sleep latency, wake after sleep onset, sleep quality in self help vs wait-list control Effect sizes small to moderate (d = 0.02 to −0.50) favoring in-person treatment vs self-help
Okajima et al,[14] 2011	14 RCTs of CBT-I vs control treatments (n = 958)	Self-report outcomes (CBT-I vs control): effect sizes small for total sleep time (d = 0.00), moderate to large for sleep latency, wake after sleep onset, total wake time, sleep efficiency (d = 0.44 to 0.86) Objective outcomes (CBT-I vs control): effect sizes small for sleep latency, total sleep time (d = 0.19-0.24), moderate for wake after sleep onset, total wake time, sleep efficiency (d = 0.42-0.73) Effects generally maintained with 3- to 12-mo follow-up
Cheng et al,[15] 2012	6 RCTs of computerized CBT-I vs waitlist or active control (n = 228)	Small to large effect sizes (d = 0.22-0.86) for sleep latency, number of awakenings, sleep efficiency, sleep quality, Insomnia Severity Index Nonsignificant effect size for wake after sleep onset (d = −0.18) Average number needed to treat in 4 studies ranges from 2.91 to 3.59
Pharmacologic treatments		
Nowell et al,[16] 1997	22 RCTs of BzRA hypnotics Adults younger than 65 y (n = 1894)	Moderate effect sizes (d = 0.56-0.71) for self-reported outcomes of sleep latency, total sleep time, number of awakenings, sleep quality *Z* scores for effect sizes range from 0.71 to 0.76
Holbrook et al,[17] 2000	45 RCTs of benzodiazepine hypnotics vs placebo or other active treatments (n = 2672)	Self-report outcomes: significant difference favoring benzodiazepines vs placebo for sleep latency, total sleep time Polysomnography outcomes: significant difference favoring benzodiazepines vs placebo for total sleep time Adverse effects (drowsiness, dizziness, lightheadedness): significantly more likely in patients taking benzodiazepines vs placebo
Smith et al,[18] 2002	21 Studies 6 Pharmacologic RCTs (n = 220 participants) 14 Behavioral RCTs (n = 250)	Moderate to large effect sizes (d = 0.46-1.20) for sleep latency, wake after sleep onset, total sleep time, sleep quality Effect size for sleep latency larger in behavioral vs pharmacologic treatment studies
Dündar et al,[19] 2004	24 RCTs comparing benzodiazepine with nonbenzodiazepine BzRA drugs Total (n = 3909)	Equivalent efficacy of benzodiazepine and nonbenzodiazepine hypnotics on most outcomes Shorter sleep latency for zolpidem vs temazepam or zopiclone and for zaleplon vs zolpidem
Glass et al,[4] 2007	24 RCTs of BzRA vs placebo Adults aged 60 or older (n = 2417)	Sleep quality: d = 0.13, number needed to treat = 13 Total sleep time: mean difference, 25.2 min (95% CI, 12.8-37.6) No. of awakenings: Mean difference, −0.63 (95% CI, −0.48 to −0.77) All adverse events: number needed to harm = 6 Significantly greater risk of cognitive, fatigue, performance adverse effects, but not psychomotor adverse events (dizziness, loss of balance), with active drugs vs placebo
Buscemi et al,[20] 2007	105 RCTs of BzRA and antidepressant drugs in chronic insomnia (n = 13 966)	Significant difference for all drugs vs placebo on polysomnographic sleep latency (weighted mean difference, −7.0 to −12.8 min) and sleep diary sleep latency (weighted mean difference, −12.2 to −19.6 min) BzRAs: significant effects on polysomnographic sleep efficiency; and on sleep diary wakefulness after sleep onset, sleep efficiency, total sleep time, sleep quality Antidepressants: significant effects on polysomnographic wake after sleep onset, sleep efficiency, total sleep time; and on sleep diary rating of sleep quality Adverse events significantly greater for BzRA and antidepressants vs placebo

Abbreviations: BzRA, benzodiazepine receptor agonist drug; CBT-I, cognitive behavioral therapy for insomnia; RCT, randomized controlled trial.
[a] The studies summarized in Table 2 are the product of a systematic literature review described in the eAppendix.

Buysee JAMA 2013;309: 706-716

Treatment: Hypnotic Reviews

Glass et al,[48] 2007	24 RCTs of BzRA vs placebo Adults aged 60 or older (n = 2417)	Sleep quality: d = 0.13, number needed to treat = 13 Total sleep time: mean difference, 25.2 min (95% CI, 12.8-37.8) No. of awakenings: Mean difference, −0.63 (95% CI, −0.48 to −0.77) All adverse events: number needed to harm = 6 Significantly greater risk of cognitive, fatigue, performance adverse effects, but not psychomotor adverse events (dizziness, loss of balance), with active drugs vs placebo
Buscemi et al,[49] 2007	105 RCTs of BzRA and antidepressant drugs in chronic insomnia (n = 13 986)	Significant difference for all drugs vs placebo on polysomnographic sleep latency (weighted mean difference, −7.0 to −12.8 min) and sleep diary sleep latency (weighted mean difference, −12.2 to −19.6 min) BzRAs: significant effects on polysomnographic sleep efficiency; and on sleep diary wakefulness after sleep onset, sleep efficiency, total sleep time, sleep quality Antidepressants: significant effects on polysomnographic wake after sleep onset, sleep efficiency, total sleep time; and on-sleep diary rating of sleep quality Adverse events significantly greater for BzRA and antidepressants vs placebo

Buysee JAMA 2013;309: 706-716

Treatment: CBT Reviews

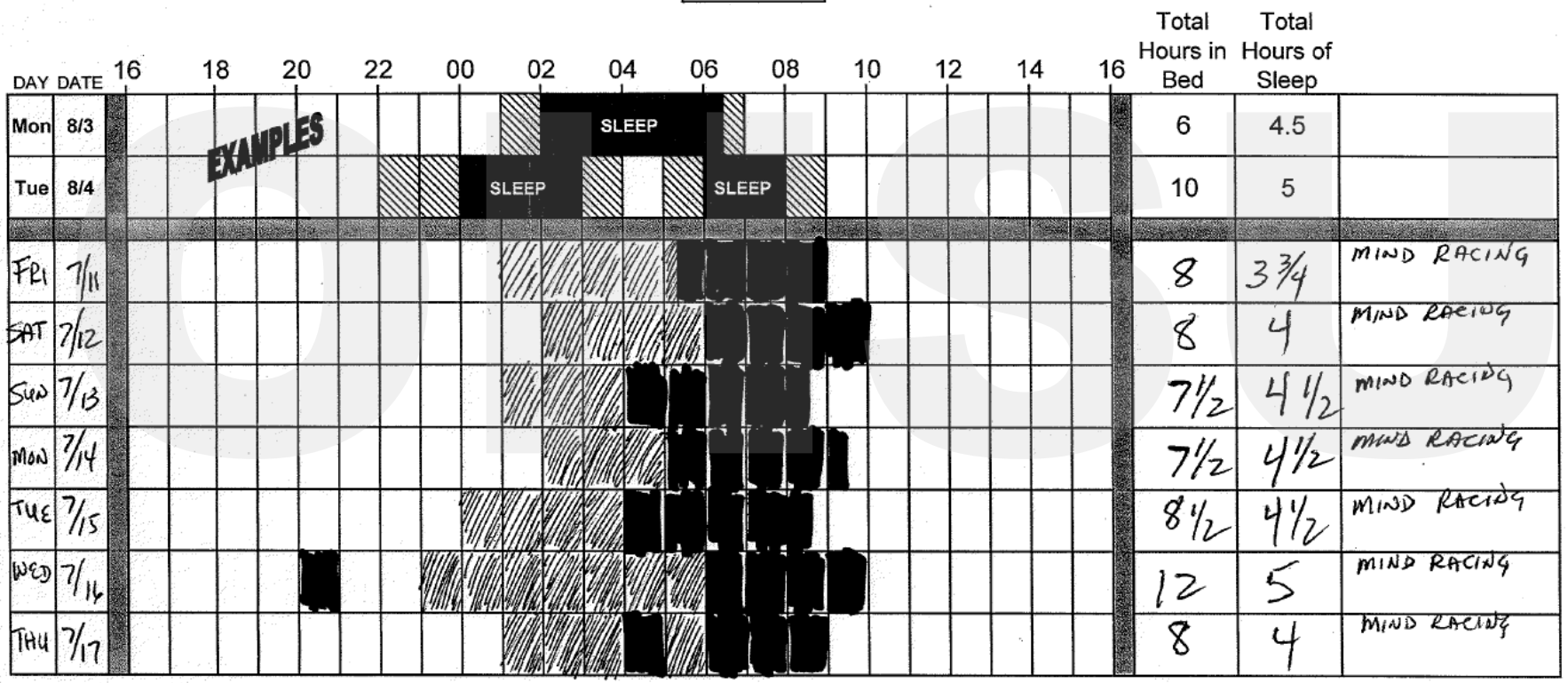
Okajima et al,[43] 2011	14 RCTs of CBT-I vs control treatments (n = 958)	Self-report outcomes (CBT-I vs control): effect sizes small for total sleep time (*d* = 0.00), moderate to large for sleep latency, wake after sleep onset, total wake time, sleep efficiency (*d* = 0.44 to 0.86) Objective outcomes (CBT-I vs control): effect sizes small for sleep latency, total sleep time (*d* = 0.13-0.24), moderate for wake after sleep onset, total wake time, sleep efficiency (*d* = 0.42-0.73) Effects generally maintained with 3- to 12-mo follow-up

Buysee JAMA 2013;309: 706-716

Case

Name [redacted]

Asleep:
In Bed Awake:
Out of Bed Awake: (leave blank)



DAY	DATE	Total Hours in Bed	Total Hours of Sleep	
Mon	8/3	6	4.5	
Tue	8/4	10	5	
FRI	7/11	8	3¾	MIND RACING
SAT	7/12	8	4	MIND RACING
SUN	7/13	7½	4½	MIND RACING
MON	7/14	7½	4½	MIND RACING
TUE	7/15	8½	4½	MIND RACING
WED	7/16	12	5	MIND RACING
THU	7/17	8	4	MIND RACING

Notes:

& propped up

IIII in bed doing other things (like watching TV)

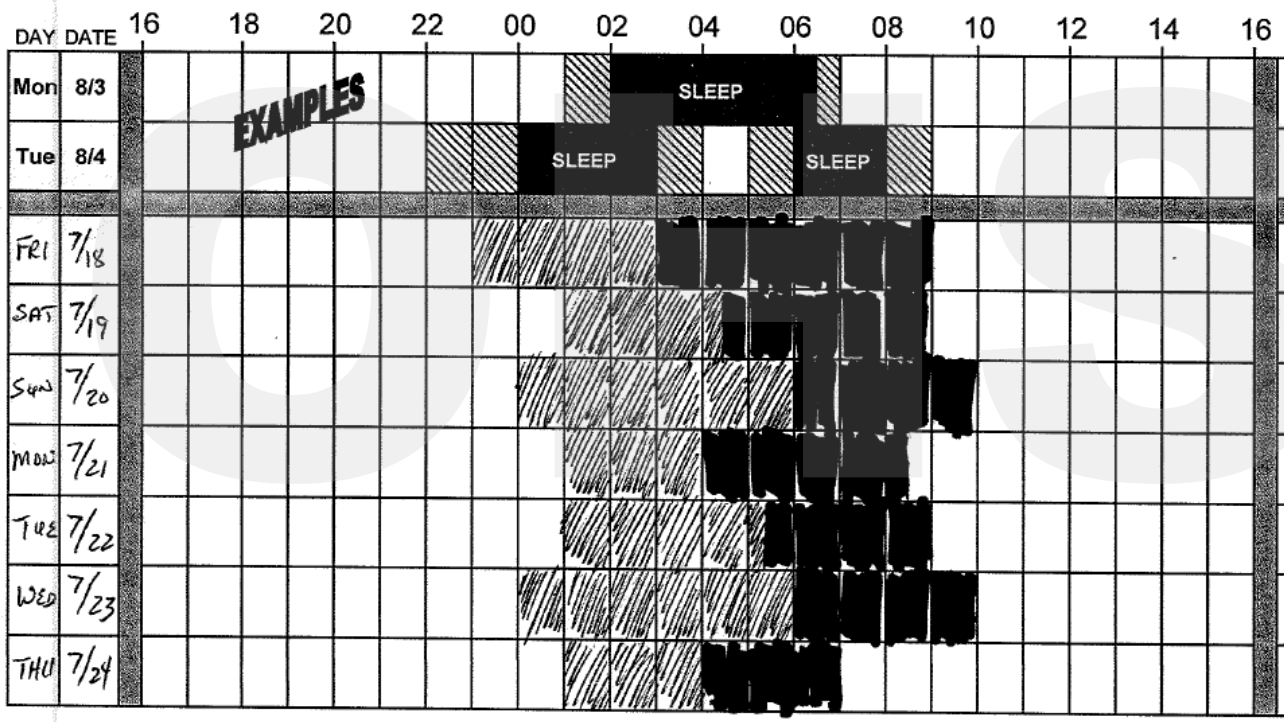
≡ in bed trying to sleep

Name: [redacted]

Asleep:

In Bed Awake:

Out of Bed Awake: (leave blank)



DAY	DATE	Total Hours in Bed	Total Hours of Sleep		
Mon	8/3	6	4.5		
Tue	8/4	10	5		
FRI	7/18	10	6	MIND RACING BEFORE GOING TO SLEEP	60%
SAT	7/19	8	4½	MIND RACING BEFORE GOING TO SLEEP.	56%
SUN	7/20	10	4	MIND RACING WATCHED A MOVIE	40%
MON	7/21	7½	4½	MIND RACING	60%
TUE	7/22	8	3½	MIND RACING	44%
WED	7/23	10	4	MIND RACING WATCHED A MOVIE	40%
THU	7/24	6	3	MIND RACING	50%

Notes:

average = 4.2 hours of sleep

3am to 9am = in bed and trying to sleep

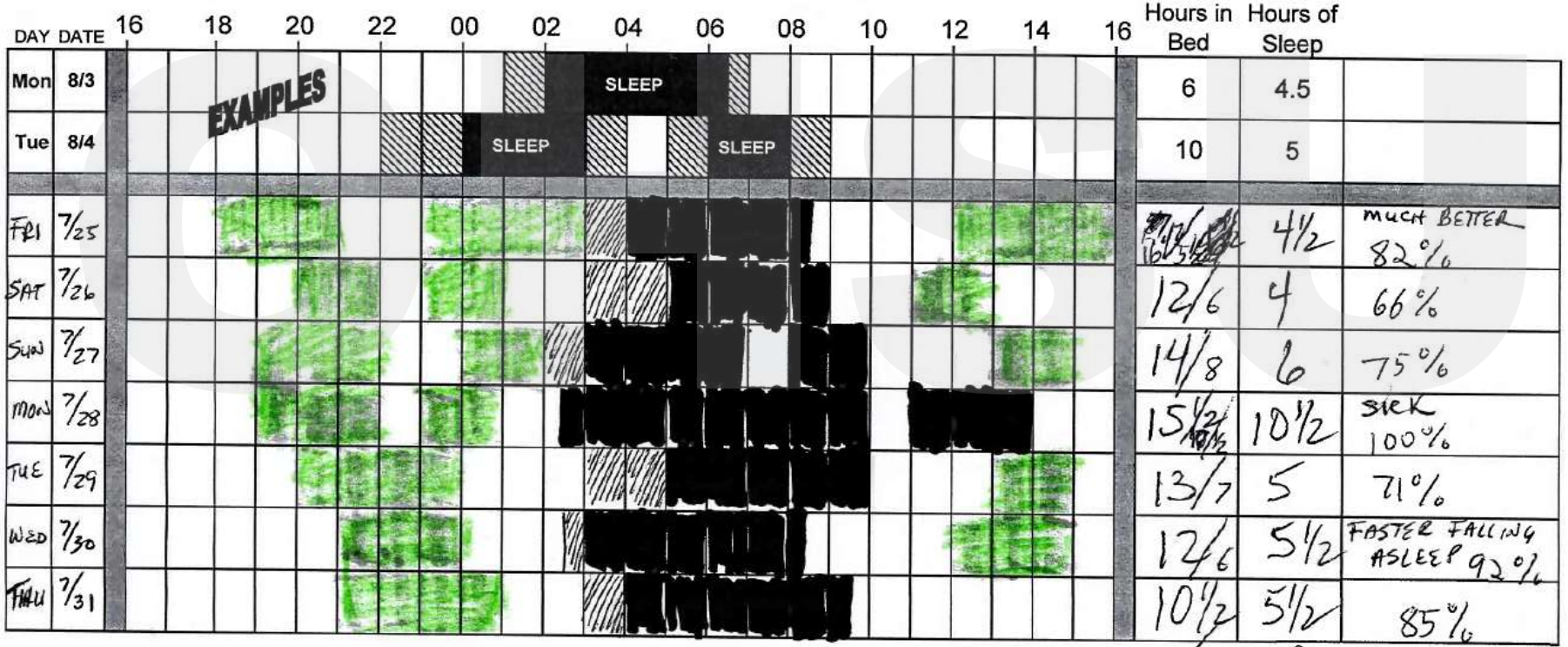
Name [redacted]

IN BED NOT TRYING TO SLEEP

Asleep:

In Bed Awake:

Out of Bed Awake: (leave blank)



DAY	DATE	NOT TRYING TO SLEEP / TRYING TO SLEEP	Total Hours in Bed	Total Hours of Sleep	
Mon	8/3		6	4.5	
Tue	8/4		10	5	
FRI	7/25		[illegible]	4½	MUCH BETTER 82%
SAT	7/26		12/6	4	66%
SUN	7/27		14/8	6	75%
MON	7/28		15½/10½	10½	SICK 100%
TUE	7/29		13/7	5	71%
WED	7/30		12/6	5½	FASTER FALLING ASLEEP 92%
THU	7/31		10½/6½	5½	85%

Notes:

average = 5.9 hours of sleep

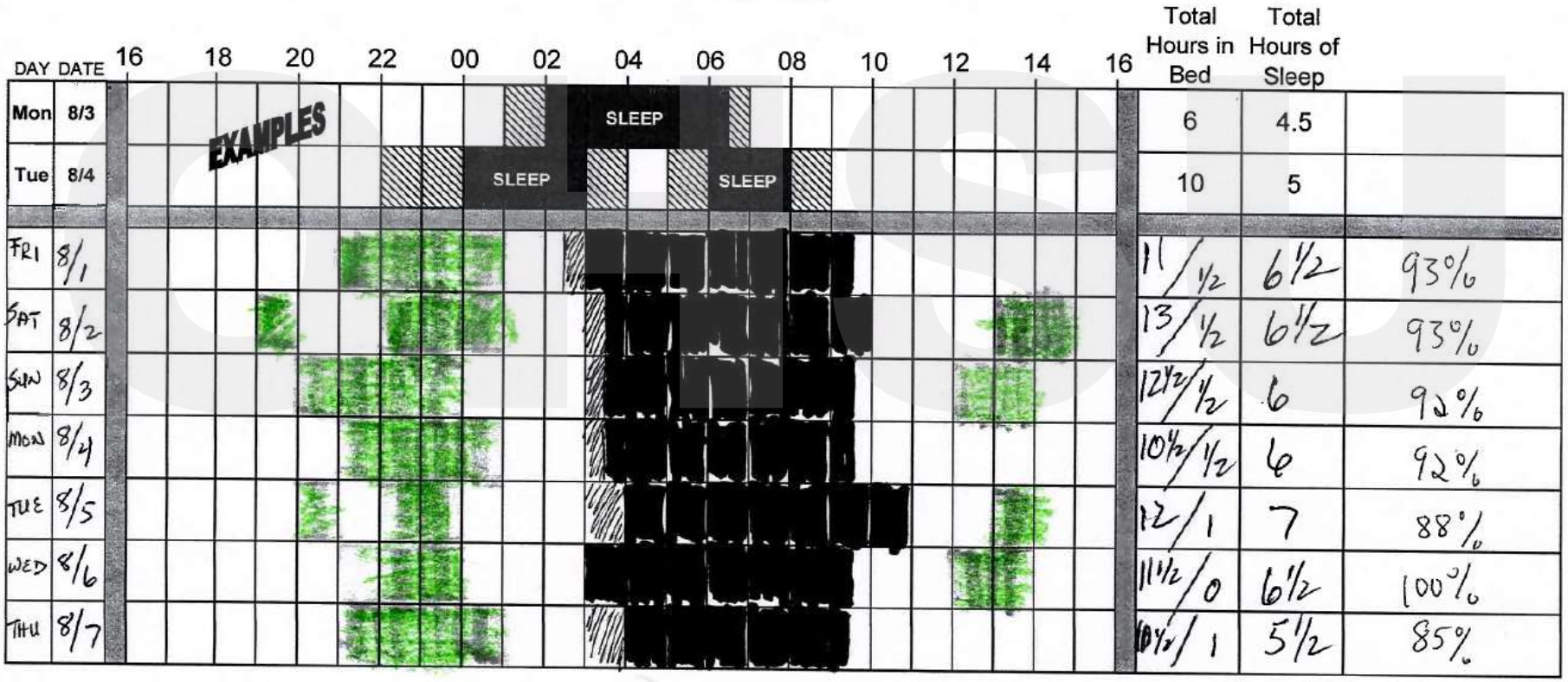
Name: [redacted]

in bed not trying to sleep: GREEN

Asleep:

In Bed Awake:

Out of Bed Awake: (leave blank)



	Total Hours in Bed	Total Hours of Sleep	
Mon 8/3	6	4.5	
Tue 8/4	10	5	
FRI 8/1	11 1/2	6 1/2	93%
SAT 8/2	13 1/2	6 1/2	93%
SUN 8/3	12 1/2	6	92%
MON 8/4	10 1/2	6	92%
TUE 8/5	12	7	88%
WED 8/6	11 1/2	6 1/2	100%
THU 8/7	10 1/2	5 1/2	85%

Notes:

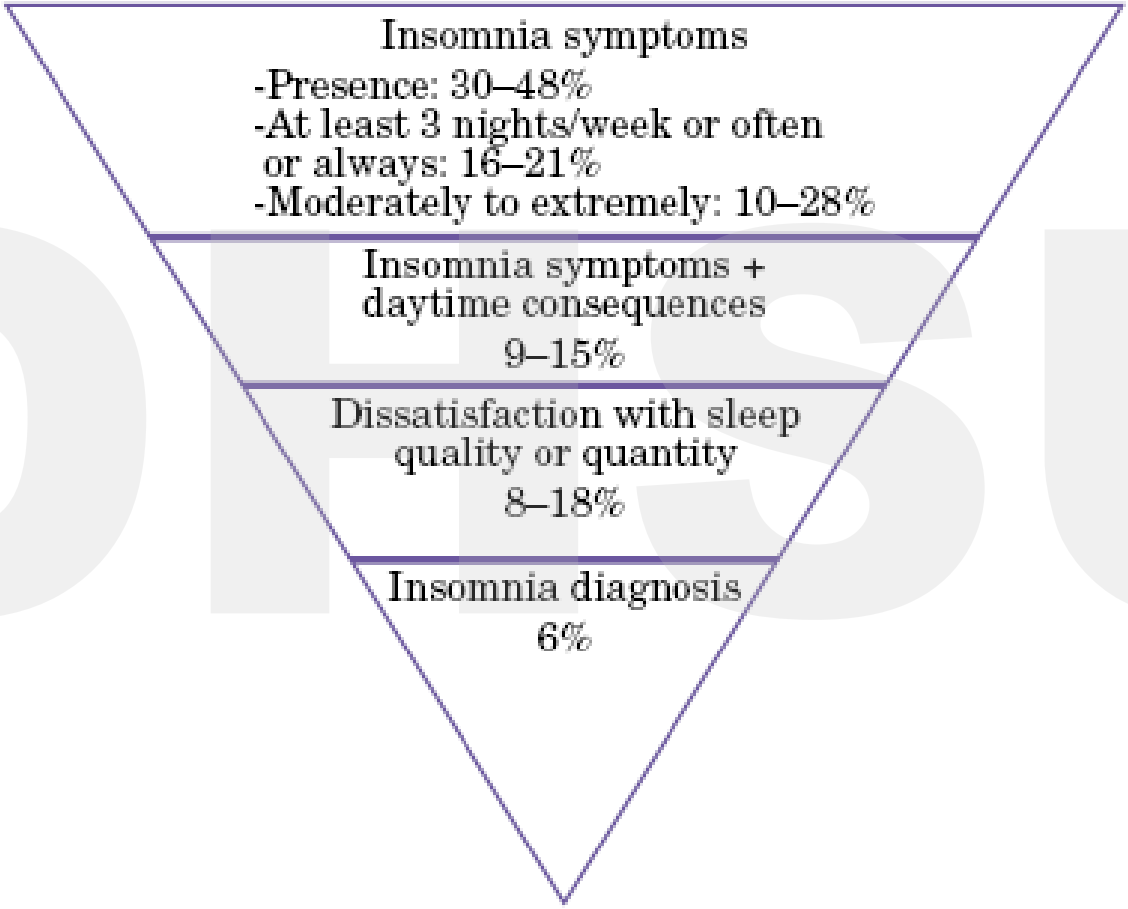
average = 6.3 hours of sleep

The End

OHSU

Extra Slides

Epidemiology



Ohayon M, Sleep Med Rev. 2002;6: 97-111
Morin CM et al., Can J Psych. 2011;56: 540-548

Epidemiology

Table 3 Prevalence of insomnia according to physical and mental health variables

	Sample description $n = 2000$		Insomnia prevalence $n = 232$						
Variable	%	*n*	%	*n*	χ^2	*df*	*P*	OR	95% CI
Self–rated physical health									
Good (reference)	84.1	1701	9.1	139	160.2	1	<0.01		
Poor	15.9	290	35.6	92				5.53	4.15–7.35
Self–rated mental health									
Good (reference)	89.4	1814	9.9	165	161.87	1	<0.01		
Poor	10.6	170	41.4	65				6.45	4.70–8.85

Ohayon M, Sleep Med Rev. 2002;6: 97-111
Morin CM et al., Can J Psych. 2011;56: 540-548

Etiology

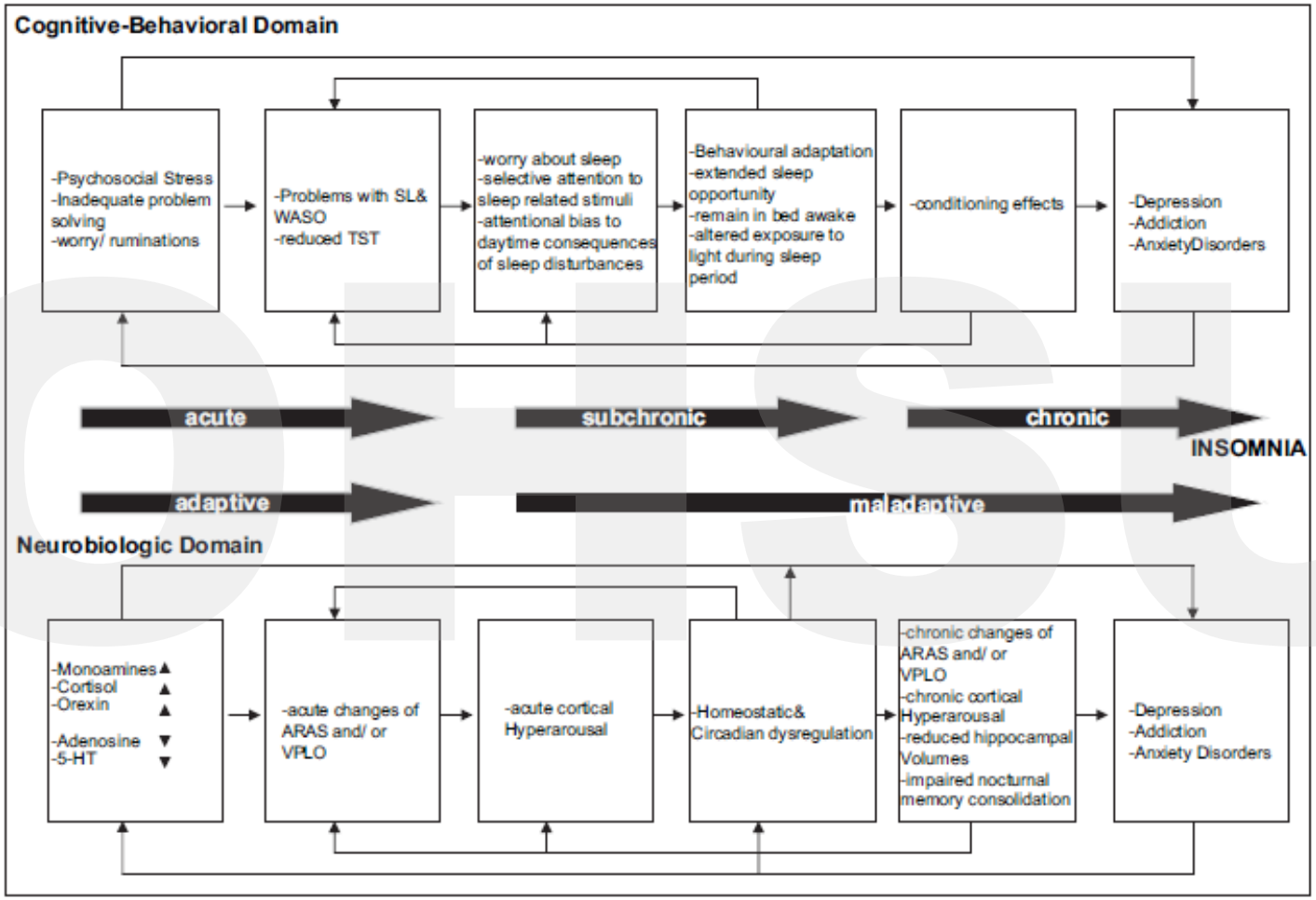


Fig. 1. Neurocognitive model of insomnia (modified according to Perlis et al., 16, 20; Pigeon and Perlis, 141). 5-HT: Serotonin; ARAS: ascending reticular activating system; SL: sleep latency; TST: total sleep time; VLPO: ventrolateral preoptic area of the hypothalamus; WASO: wake after sleep onset. Acute insomnia: 1–90 days; subchronic: 3–6 months; chronic >6 months. Note: the cognitive-behavioral and the neurobiologic domain are depicted in a parallel way – it is assumed (see text) that both domains are strongly interconnected and not independent of each other.

Reimann et al. Sleep Med Rev 2010;14: 19-31

BzRAs: Effects

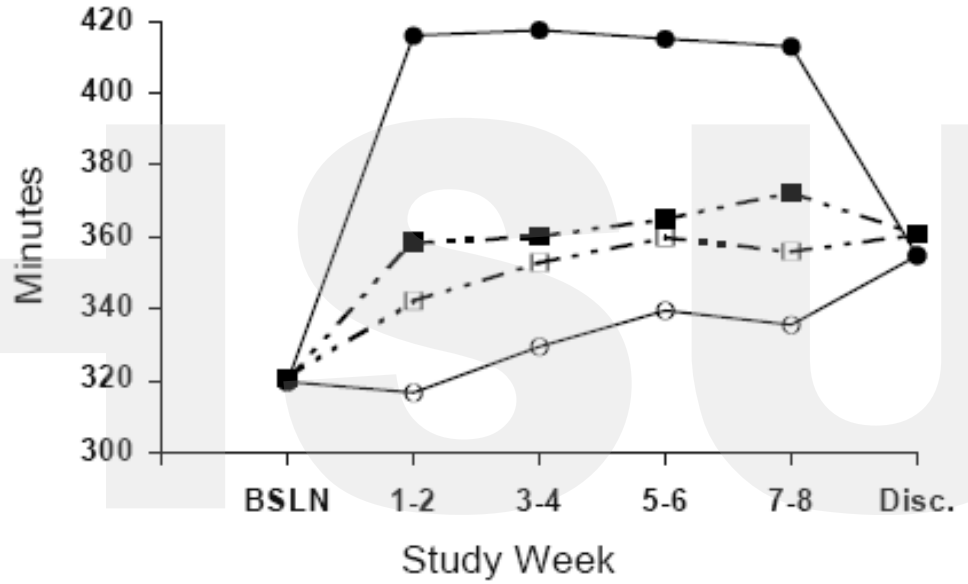


Figure 4—Mean subjective total sleep time for zolpidem-pill nights (solid line/solid symbol), zolpidem-no pill nights (solid line/open symbol), placebo-pill nights (dashed line/solid symbols), and placebo-no pill nights (dashed line/open symbols), for each study period (see Table 5 for statistical comparisons).

Treatment: Pharmacologic

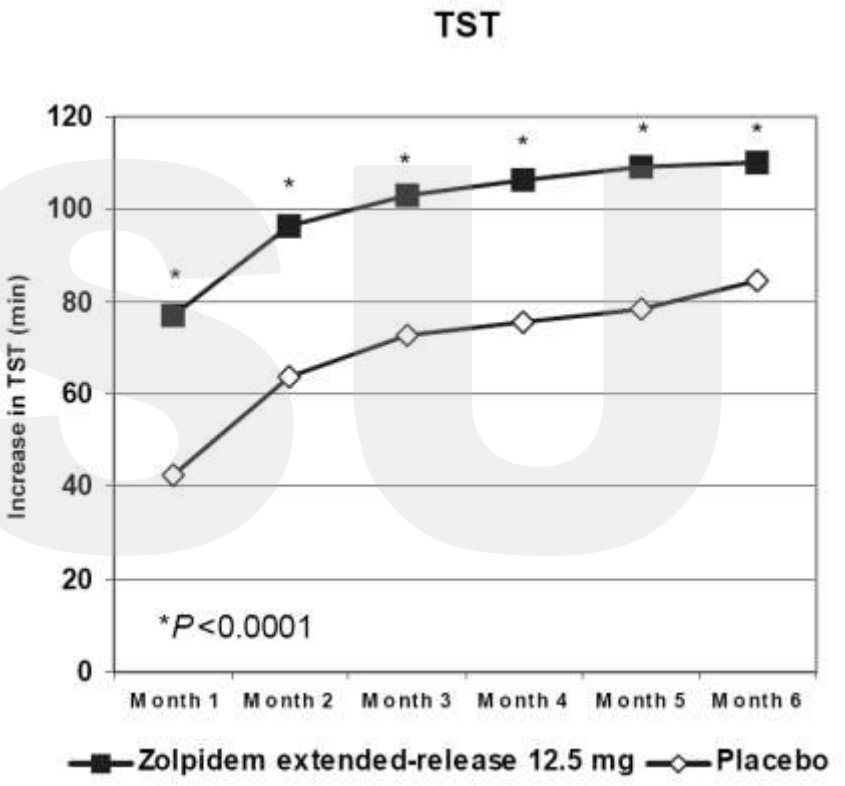
- Benzodiazepine Receptor Agonists (BzRAs)
  - Benzodiazepines
  - Non-Benzodiazepines $GABA_A$ agonists
- Sedating Antidepressants
- Sedating Antipsychotics
- Antihistamines
- Suvorexant (orexin antagonist)
- Gamma-Hydroxybutyrate (GHB)
- Melatonin and Melatonin agonists, Gabapentin, Valerian

Treatment: Pharmacologic

- Benzodiazepine Receptor Agonists (BzRAs)
  - Benzodiazepines
  - Non-Benzodiazepines $GABA_A$ agonists: zolpidem, zaleplon, eszopiclone
- Sedating Antidepressants
- Sedating Antipsychotics
- Antihistamines
- Suvorexant (orexin antagonist)
- Gamma-Hydroxybutyrate (GHB)
- Melatonin and Melatonin agonists, Gabapentin, Valerian

BzRAs: zolpidem ER

- 12.5 mg of zolpidem ER increased total sleep time (sleep diary) by ~110 minutes over 6 months
- Placebo increased total sleep time by ~85 minutes
- Difference of ~25 minutes



Krystal AD et al., Sleep. 2008;31:79-90.

BzRAs: benzodiazepines

- 15 mg of temazepam increased total sleep time (sleep diary) by 1.0 hours over 2 weeks
- Placebo increased total sleep time by 0.4 hours
- Difference of 0.6 hours

TABLE 1. Summary of Results for Sleep Quality, Sleep-Onset Latency, Number of Awakenings, and Total Sleep Time

	Baseline, mean (SD)	Placebo, mean (SD)	Diphenhydramine, mean (SD)	Temazepam, mean (SD)
Sleep quality (n = 19) (scales, 1–5)	2.5 (0.77)	2.9 (0.77)*	3.0 (0.81)	3.3 (0.86)†,‡
Sleep-onset latency (n = 19), min	55.8 (39.0)	36.8 (24.8)	34.2 (22.7)	25.4 (21.5)†
No. awakenings (n = 19)	2.0 (1.3)	2.0 (1.2)	1.7 (1.1)†	1.5 (1.3)†
Total sleep time (n = 19), h	5.9 (1.7)	6.3 (1.3)	6.6 (1.3)	6.9 (1.0)†

*$P < 0.05$ compared with baseline.
†$P < 0.05$ compared with placebo.
‡$P < 0.05$ compared with diphenhydramine.

Glass et al. J Clin Psychopharm 2008; 28: 182-188

Treatment: Pharmacologic

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  - Benzodiazepines
  - Non-Benzodiazepines $GABA_A$ agonists
- Sedating Antidepressants
- Sedating Antipsychotics
- Antihistamines
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- Gamma-Hydroxybutyrate (GHB)
- Melatonin and Melatonin agonists, Gabapentin, Valerian

Sedating Antidepressants: Doxepin

- 3 mg of doxepin increased total sleep time (PSG) by 46.8 minutes over 3 months
- Placebo increased total sleep time by 23.1 minutes
- Difference of 23.7 minutes

Table 2—Effect of doxepin and placebo on PSG sleep onset, sleep maintenance, and early morning awakening parameters

Measure	Baseline		Night 1		Night 29		Night 85	
TST (min)	Mean	(SD)	Mean	(SD)	Mean	(SD)	Mean	(SD)
Placebo	320.6	(40.3)	339.7	(54.4)	345.0	(59.1)	343.7	(57.7)
DXP 1 mg	322.4	(39.9)	359.1*	(53.1)	344.4	(55.1)	360.5*	(47.2)
DXP 3 mg	326.9	(33.2)	382.9***	(44.2)	363.9*	(54.0)	373.7***	(42.2)

Krystal, et al. Sleep 2010; 33:1553-61

Treatment: Pharmacologic

- Benzodiazepine Receptor Agonists (BzRAs)
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  - Non-Benzodiazepines $GABA_A$ agonists
- Sedating Antidepressants
- Sedating Antipsychotics
- Antihistamines
- Suvorexant (orexin antagonist)
- Gamma-Hydroxybutyrate (GHB)
- Melatonin and Melatonin agonists, Gabapentin, Valerian

Gimenez et al. Psychopharm 2007; 190: 507-516
Tassniyom et al. J Med Assoc Thai 2010; 93: 729-34

Antipsychotics

- 25 mg of Quetiapine increased total sleep time (sleep diary) by 124.9 minutes over 2 weeks
- Placebo increased total sleep time by 72.2 minutes
- Difference of 52.7 minutes

	Placebo Mean (SD)	Quetiapine Mean (SD)	p-value
Total sleep time (minutes)			
Before treatment	289.64 (67.90)	222.55 (142.93)	
After treatment	361.88 (85.37)	347.47 (100.87)	
Differences between before and after	72.24 (45.02)	124.92 (82.90)	0.193

Tassniyom et al. J Med Assoc Thai 2010; 93: 729-34

Treatment: Pharmacologic

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- Sedating Antidepressants
- Sedating Antipsychotics
- Antihistamines
- Suvorexant (orexin antagonist)
- Gamma-Hydroxybutyrate (GHB)
- Melatonin and Melatonin agonists, Gabapentin, Valerian

Antihistamines: diphenhydramine

- 50 mg of diphenhydramine increased total sleep time (sleep diary) by 0.7 hours over 2 weeks
- Placebo increased total sleep time by 0.4 hours
- Difference of 0.3 hours

TABLE 1. Summary of Results for Sleep Quality, Sleep-Onset Latency, Number of Awakenings, and Total Sleep Time

	Baseline, mean (SD)	Placebo, mean (SD)	Diphenhydramine, mean (SD)	Temazepam, mean (SD)
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*$P < 0.05$ compared with baseline.
†$P < 0.05$ compared with placebo.
‡$P < 0.05$ compared with diphenhydramine.

Glass et al. J Clin Psychopharm 2008; 28: 182-188

Treatment: Pharmacologic

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- Gamma-Hydroxybutyrate (GHB)
- Melatonin and Melatonin agonists, Gabapentin, Valerian

Orexin antagonist

- Suvorexant (30 or 40 mg) increased total sleep time (sleep diary) by 38.7 minutes over one month
- Placebo increased total sleep time by 16.0 minutes
- Difference of 22.7 minutes

	Suvorexant, N=517*	Placebo, N=254*	Difference	p value
sTST				
Week 1	41·1 (36·9 to 45·3)	14·1 (8·2 to 20·1)	27·0 (19·7 to 34·3)	<0·0001
Week 2	32·4 (28·1 to 36·7)	14·7 (8·6 to 20·8)	17·7 (10·2 to 25·2)	<0·0001
Week 3	39·6 (35·3 to 44·0)	16·4 (10·3 to 22·6)	23·2 (15·6 to 30·7)	<0·0001
Week 4	41·6 (37·1 to 46·1)	18·7 (12·3 to 25·1)	22·9 (15·0 to 30·7)	<0·0001
Month 1, average weeks 1–4	38·7 (35·0 to 42·3)	16·0 (10·8 to 21·2)	22·7 (16·4 to 29·0)	<0·0001

Michelson et al. Lancet Neurol 2014; 13: 461-471

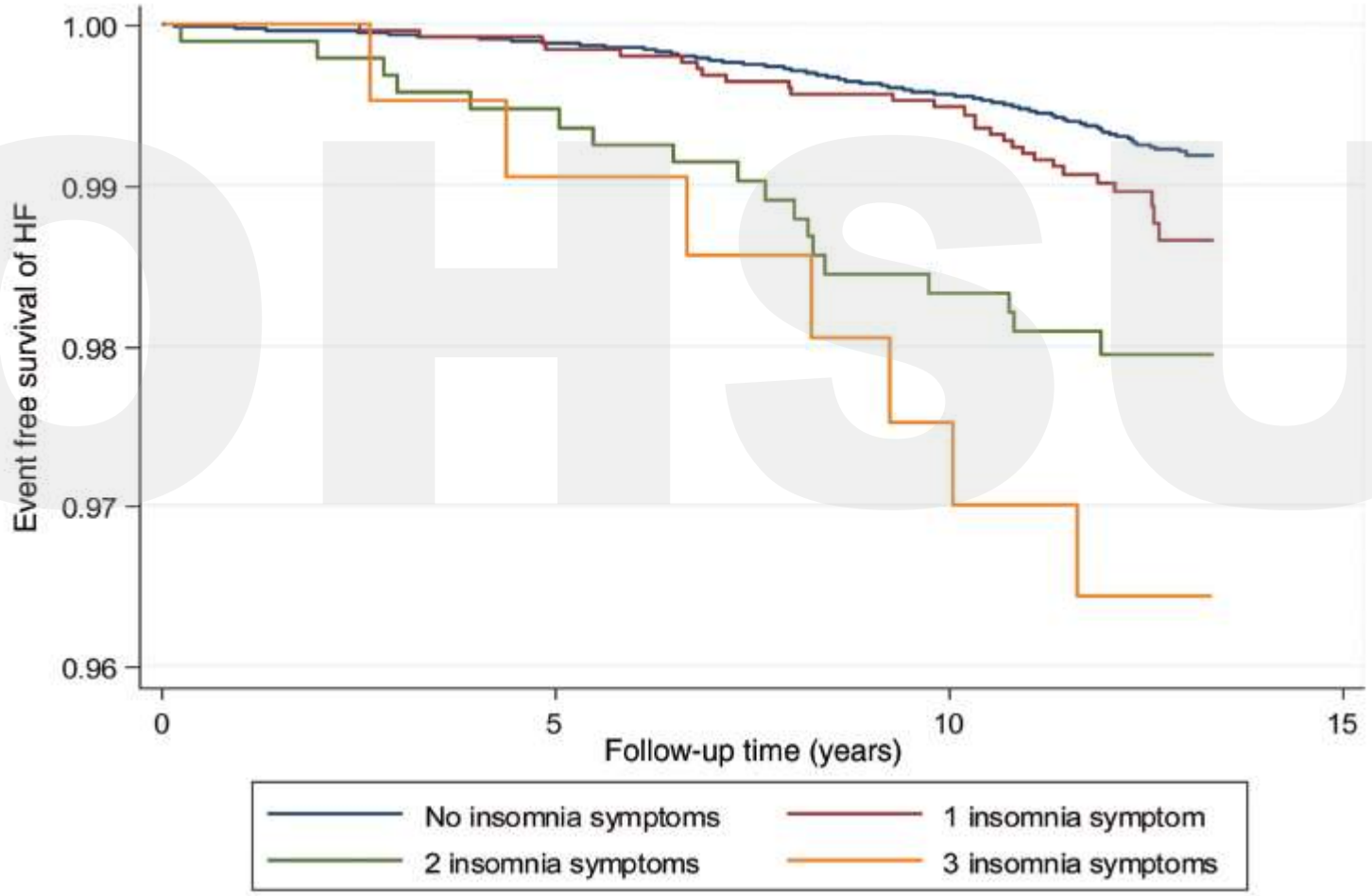
Orexin antagonist

- Suvorexant of 3 different doses, one night PSG
- Placebo total sleep time 440.65 minutes
- Suvorexant total sleep time of up to 461.40 minutes
- Difference of 20.75 minutes

Endpoints	Treatment	Raw value		Geometric mean[1]		Geometric mean ratio[1] (suvorexant vs. placebo)	
		Mean	SD	Mean	95% CI	Mean	90% CI
TST (min)	Placebo	440.65	17.32	440.32	(433.87, 446.86)	–	–
	10 mg	448.26	18.07	447.70	(441.00, 454.49)	1.02	(1.00, 1.03)
	50 mg	458.90	10.18	458.79	(452.07, 465.61)	1.04	(1.03, 1.06)
	100 mg	461.40	9.55	461.30	(454.55, 468.16)	1.05	(1.03, 1.06)

Sun et al. Sleep 2013;356:259-267

Morbidity/Co-Morbidity: Heart Failure



Laugsand et al., Euro Heart J 2013; 124: 2073-2081

Treatment: Comparisons

- Similar efficacy pharmocologic vs. cognitive-behavioral treatments in several studies
- 8 weeks of CBT vs. temazepam (7.5-30 mg) vs. combined treatment. CBT maintained improved sleep at 3, 12, and 24 months.
- ~6 weeks of CBT vs. zolpidem (5-10mg) vs. combined treatment. CBT generally better than zolpidem.

Morin CM, et al. JAMA 1999;281:991-9
Jacobs GD, et al. Arch Intern Med 2004;164:1888-1896
Morin CM, et al. Sleep 2006;29:1398-1414

Treatment: Comparisons

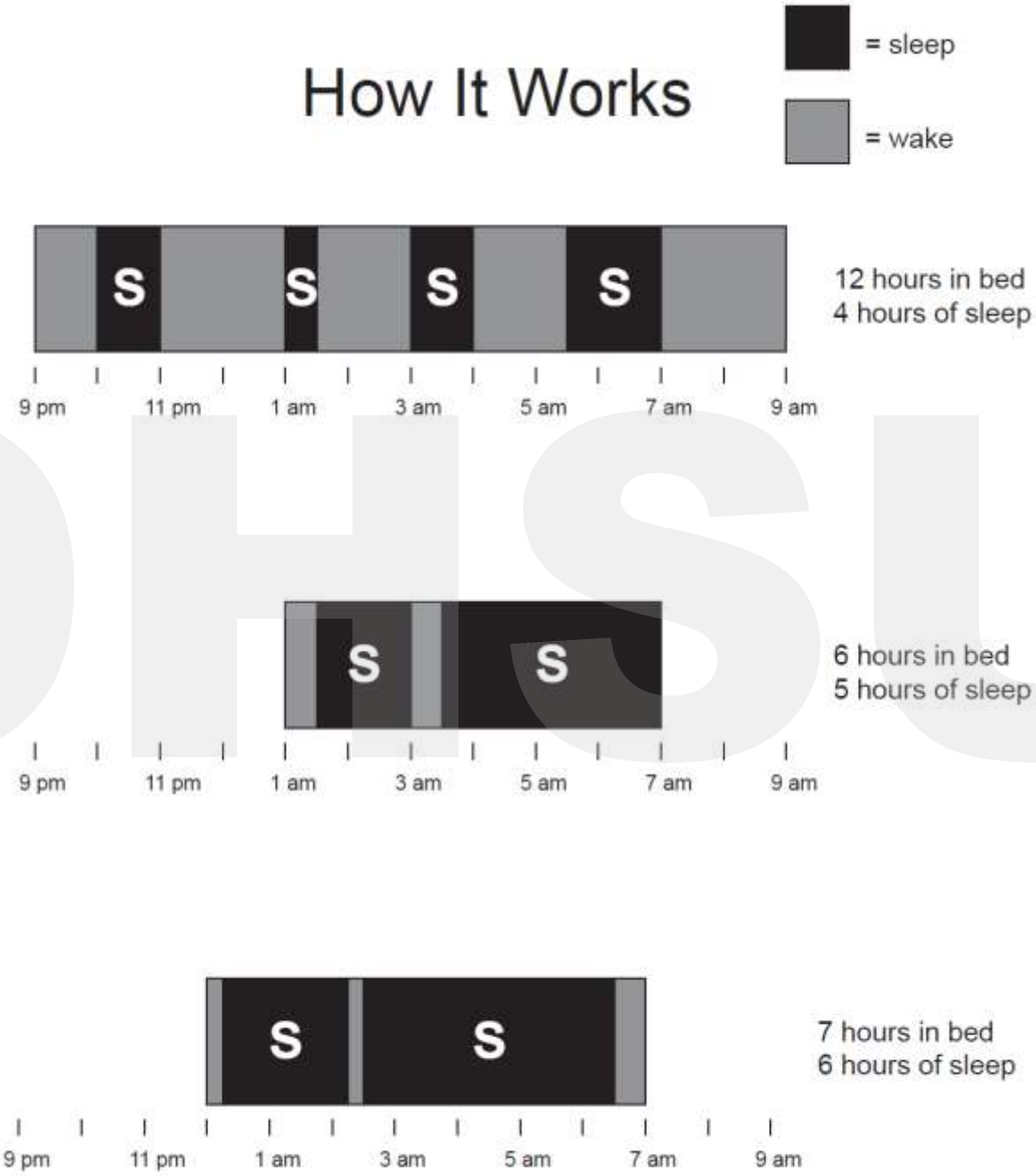
- 6 weeks of: zolpidem (10 mg x 4 wks, 5 mg x 1 wk, 5 mg q o night x 1 wk), placebo, or CBT-I (4x30 min. and 1x15 min sessions). Sleep diary (2 weeks).
- zolpidem increased total sleep time by 39.7 minutes after 4 weeks (vs 69.2 minutes after taper)
- CBT-I increased total sleep time by 48.6 minutes
- Placebo increased total sleep time by 29.5 minutes

Table 3. Sleep Latency, Sleep Efficiency, and Total Sleep Time*

Assessment Modes	CBT	Pharmacotherapy	Combination Therapy	Placebo
Total sleep time, min				
Sleep diary				
Before treatment	306.6 (70.2) (n = 15)	303.7 (60.9) (n = 15)	341.6 (68.5) (n = 18)	291.7 (89.5) (n = 15)
Midtreatment	347.4 (46.8) (n = 14)	343.4 (76.8) (n = 14)	351.3 (69.4) (n = 12)	296.8 (99.6) (n = 14)
After treatment	355.2 (44.4) (n = 14)	372.9 (83.7) (n = 13)	366.9 (80.5) (n = 13)	321.2 (76.7) (n = 14)

Jacobs GD, et al. Arch Intern Med 2004;164:1888-1896

How It Works



RADICAL ACCEPTANCE

"Radical Acceptance" means acknowledging what **already** is.

"Radical Acceptance" doesn't mean that you like or approve of the situation. It doesn't mean it's fair, or the way things "should" be. It doesn't mean that the situation is any less bad than you think it is.

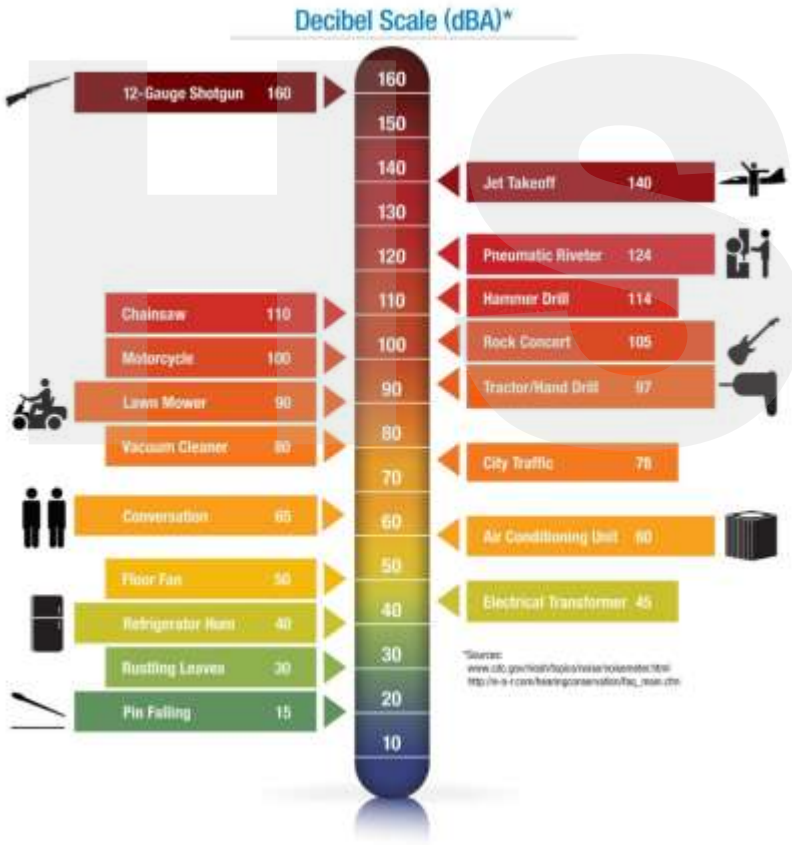
Radical acceptance simply means that you stop fighting reality. By accepting reality, acknowledging the way things are, we then have a basis for defining what the options are, and making a plan to change the things we have the power to change.

By accepting reality, we can stop wasting energy trying to change the things we cannot change.

Radical acceptance IS difficult – but it's worth the effort.

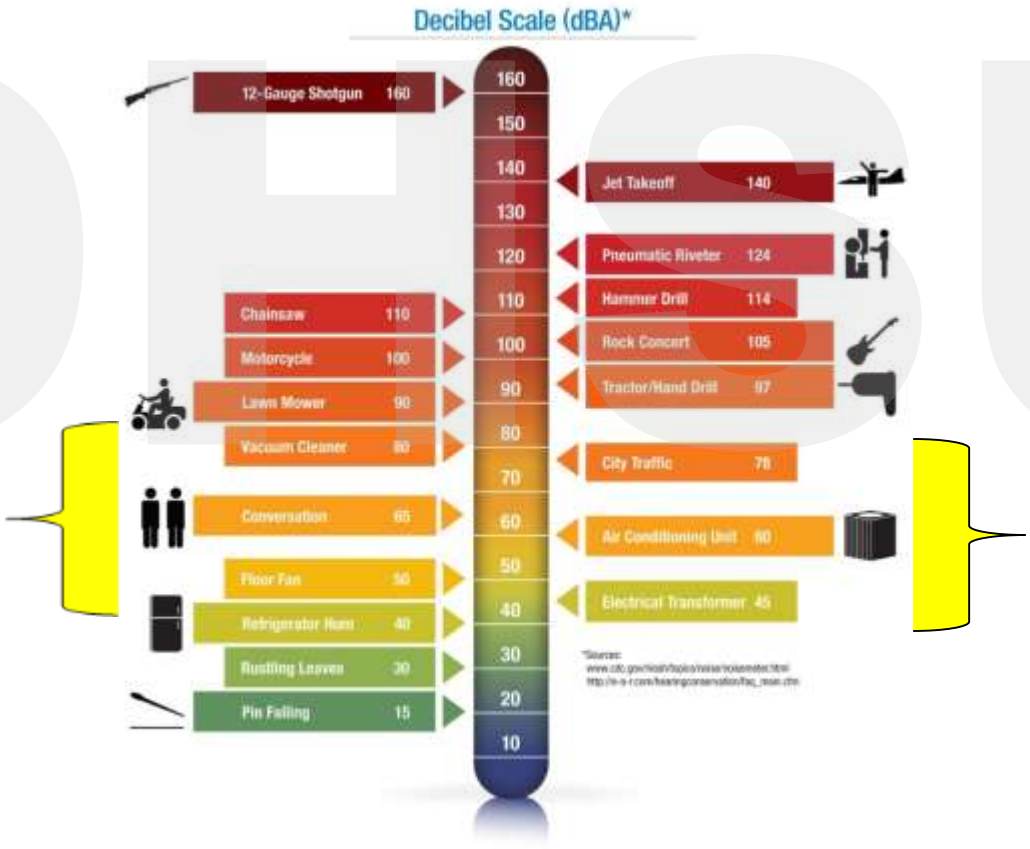
Accepting reality can bring us peace of mind, even when the situation is bad.

Sensory Processing During Sleep



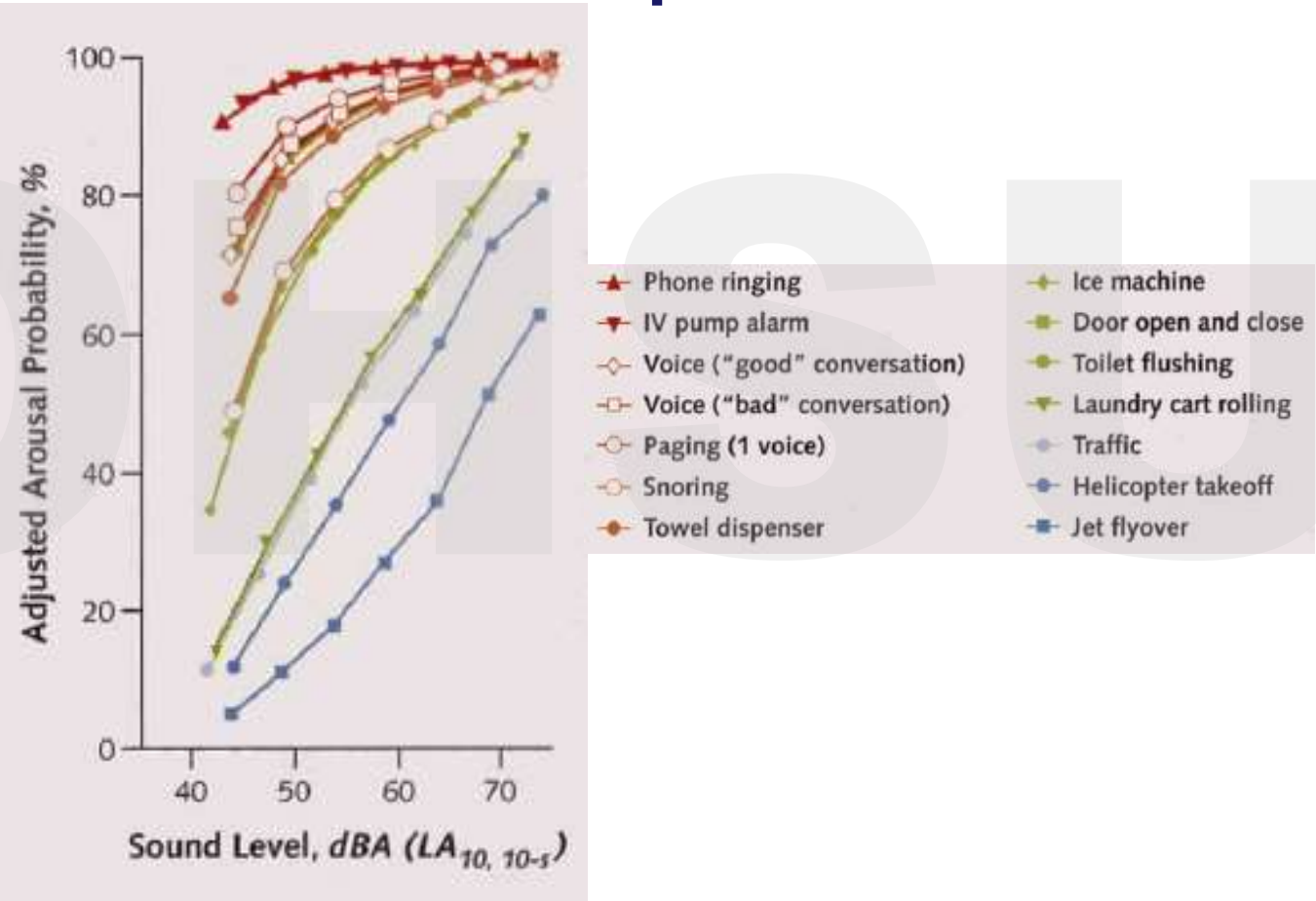
Buxton et al., Ann Intern Med. 2012;157: 170-179

Sensory Processing During Sleep



Buxton et al., Ann Intern Med. 2012;157: 170-179

Sensory Processing During Sleep



Buxton et al., Ann Intern Med. 2012;157: 170-179

Antidepressant Efficacy

Starting HAM-D_{17} score of ~20

HAM-D_{17}:
8-13 = mild
14-18 = moderate
≥ 19 = severe

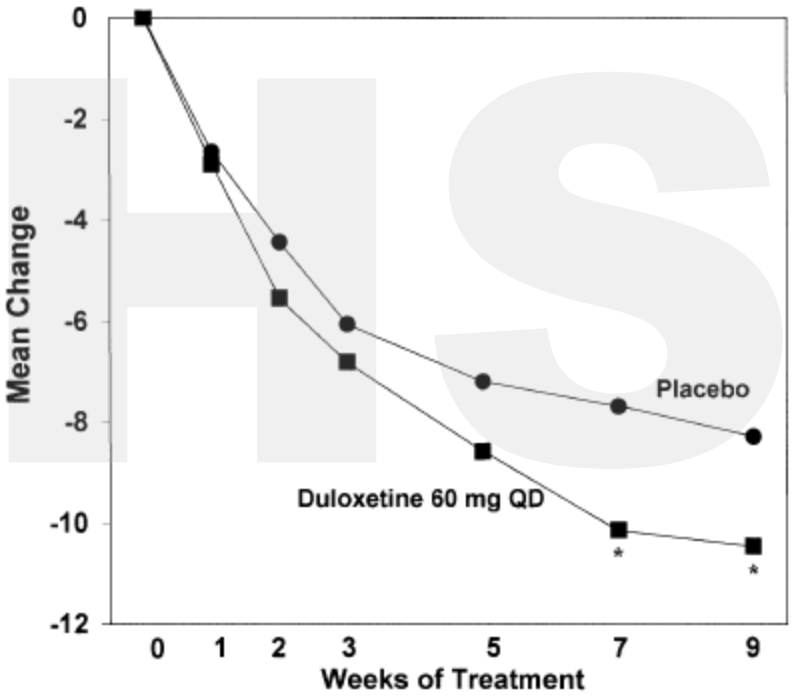


Fig. 1. Effect of placebo ($n = 139$) and duloxetine 60 mg QD ($n = 128$) on $HAMD_{17}$ total score (mean change from baseline). $^*P < .05$ for duloxetine vs. placebo.

-8.3

-10.5

Detke MJ et al., J. of Psychiatric Res. 2002; 36:383-390.