

SLEEP ISSUES AND TREATMENT

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Points to keep in mind:

- THE “PRACTITIONER CLAUSE”: Theory and practice aren’t always the same!
- A patient’s perception of sleep quality is not always accurate.
- Behavioral and health issues should be considered first.
- Benzodiazepines are a last resort.
- This lecture will focus on the practice of treating sleep issues.
- Patient response is unpredictable!

• Why learn about sleep?

- Improved wound healing—deprivation shown to cause drop in WBC's.
- Changes in performance on cognitive tests and simulated driving
- Increased cortisol levels from less sleep
- Impacts brain size and development in young children (Mirmiran et al, '83)
- Study of 1 million subjects found 15% incr. mortality risk in >9 or <4 hrs of sleep.
- Attention, mood, psychiatric status affected.

Causes: EVERYTHING!

Medications

Substance abuse

Thyroid

Psychiatric conditions

Pain

Sleep apnea

Autoimmune illness

Deconditioning

Stress

Poor sleep habits

Pulmonary condition

Bladder problems

Environment

Cardiac

Neurological

Infections

Sleep Stages are divided into REM and NREM on a Polysomnogram



STAGES OF NREM:

- STAGES:
 - **N1:** light sleep—alpha waves on EEG
 - **N2:** distinct EEG changes—sleep spindles
 - **N3:** Restorative sleep. Delta or Slow Wave Sleep (SWS).
 - SWS affects release of GH—subjects with high amt of SWS (24%) had elevated GH. Subjects with low amt. (9%) had low GH. (Turner, Drummond, Salamat, Brown)

Stages of sleep: NREM

- RESTORATIVE sleep occurs here.
- HR, BP, RR, brain activity and metabolism all drop during this phase..
- Occurs in 90-120 min cycles before REM
- Disoriented when awakened.
- Night terrors occur in this phase
- Plays a role in declarative memory
- Assoc. w/ many parasomnias

Factors that affect SWS:

- Antidepressants and 2nd generation antipsychotics may increase this by decreasing REM sleep.
- Shown to be increased by trazadone, neurontin, lyrica and GHB (xyrem).
- Shows a rebound increase after sleep deprivation.
- Decreased by steroids and possibly antihistamines.
- Increased by starvation and exercise.
- Rebound decrease from benzodiazepines

REM

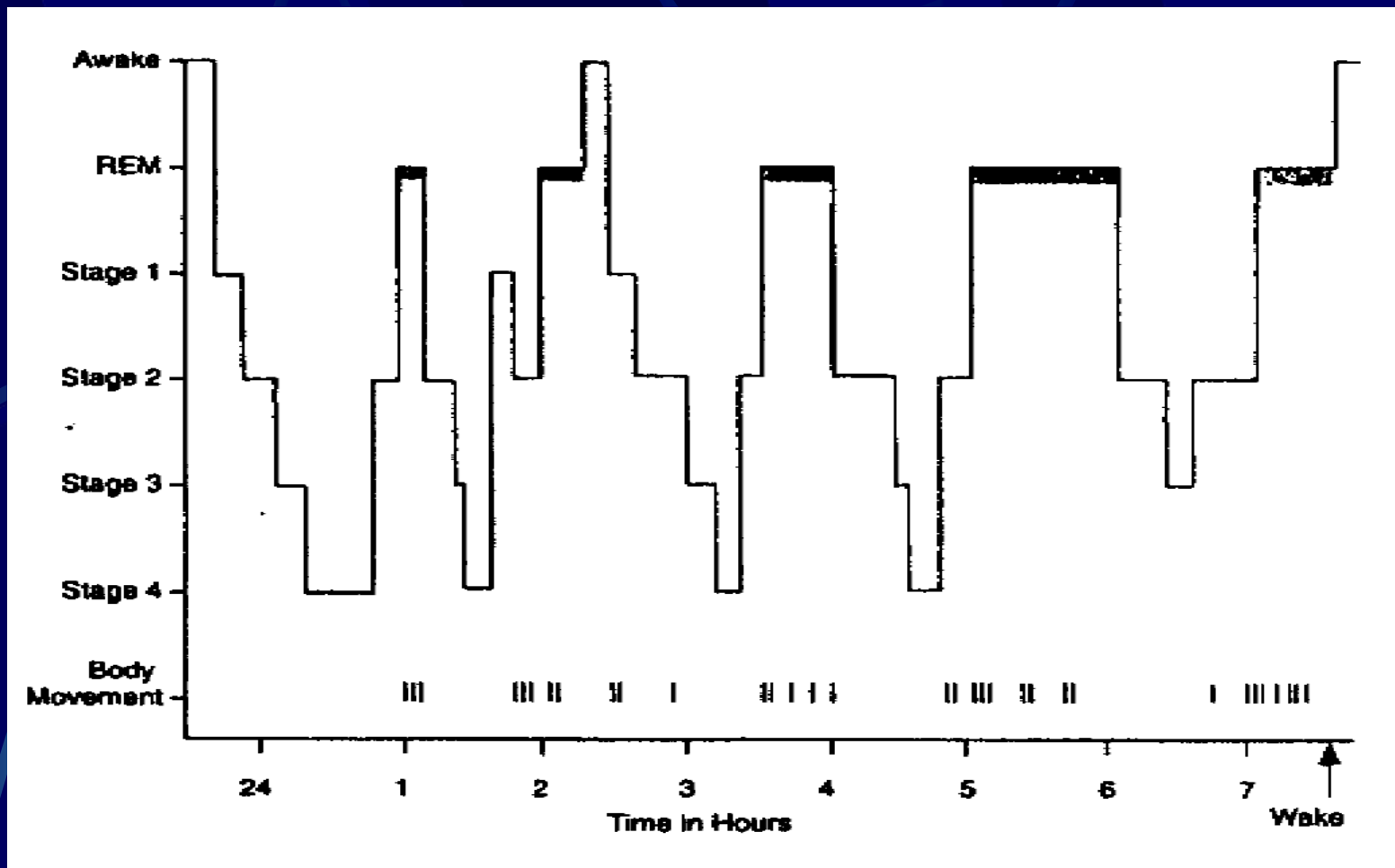
- Traditionally thought of as “dream sleep”
- Similar to wakefulness on EEG.
- Period of high brain activity and O₂ use.
- INCREASES in depression, stress, learning & anxiety.
- Muscle paralysis
- KEY POINT: >REM = <NREM, therefore, less restorative sleep.
- Plays a role in procedural memory.
- Newborns spend 80% sleep in REM.
Adults ~25%

More Facts on REM

- Dreaming found to be stimulated by the PONS and displayed random activity in the cerebral cortex. Explains why dreams are irrational and tangential. May play a role in problem-solving and desensitization of trauma. Activates the limbic system.
- Decreased by ETOH, benzo's and barbituates but rebounds by late night.
- Decreased by antidepressants

AVERAGE SLEEP PATTERNS

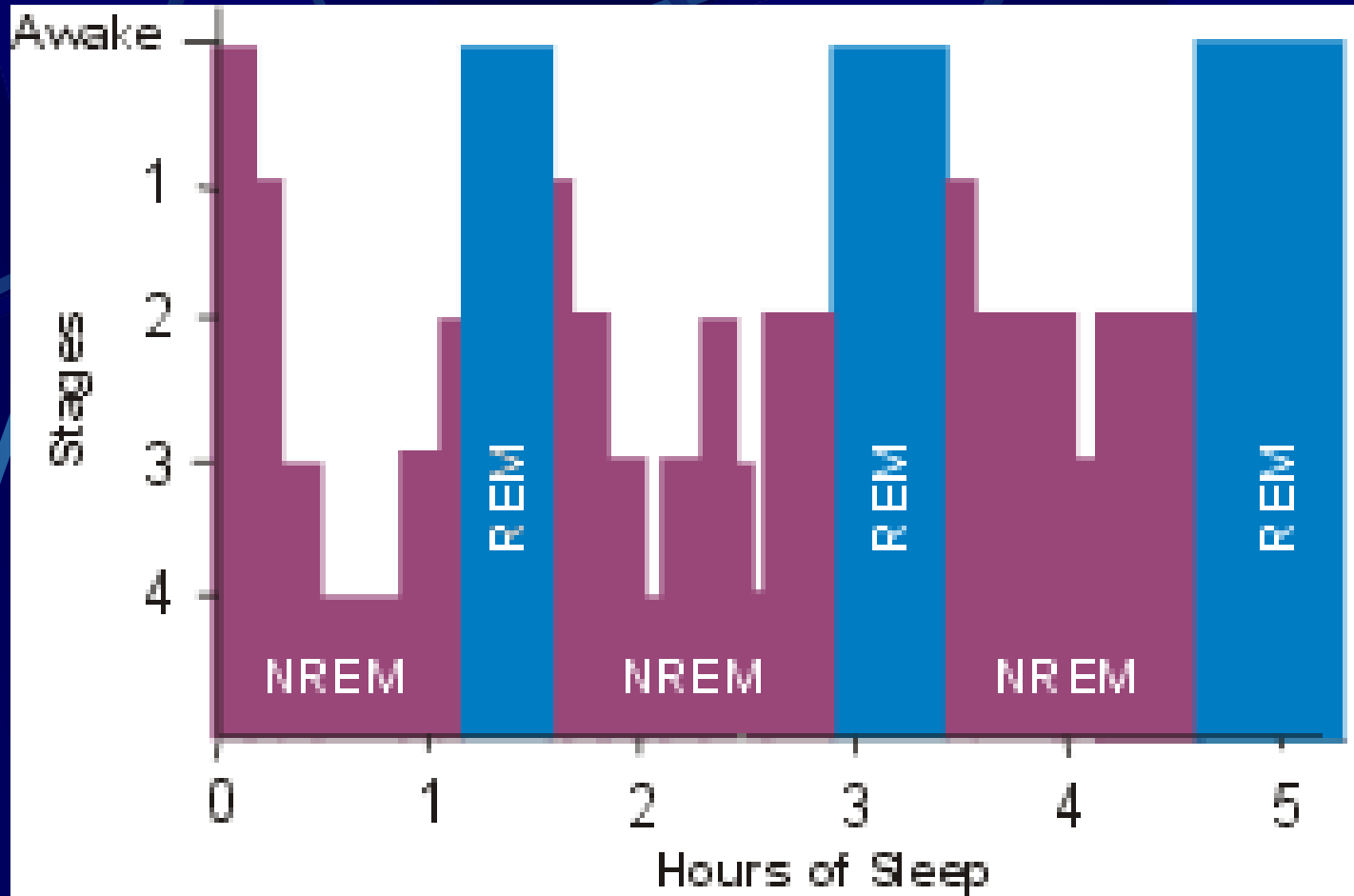
- STAGE 1: 5%
- STAGE 2: 45%
- STAGE 3: 12%
- STAGE 4: 13%
- REM: 25%
- Changes due to many conditions.
- Regulation is thought to occur in the brainstem where neurotransmitters are produced.



"Normal" sleep cycle

NREM predominant in first half of night

REM predominant in second half



Sequences of states and stages of sleep

NEUROTRANSMITTERS:

SEROTONIN: Low serotonin reduces sleep. Pre-cursor: Tryptophan incr. sleep and decr. awakenings.

*Tryptophan -> Serotonin-> Melatonin

NOREPINEPHRINE: >NE= <REM.

Assoc. w/ alertness (amphetamines).

Reserpine, that <NE causes depression and severe nightmares.

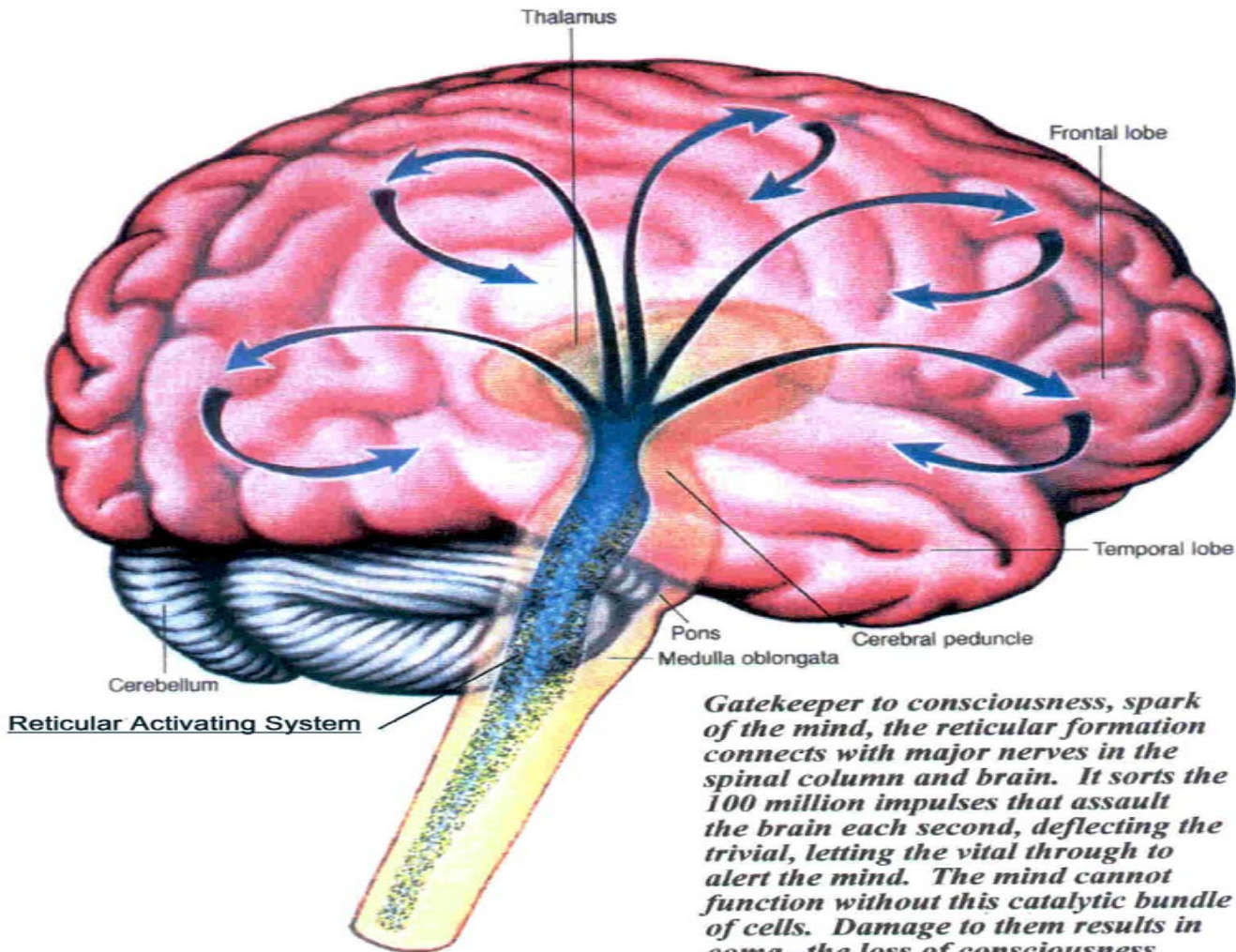
NEUROTRANSMITTERS:

- ACETYLCHOLINE:
- PARASYMPATHETIC.
- Injections of cholinergic drugs into sleep centers in rat brains caused them to go into REM
- People w/ depression may either have higher amts or a sensitivity to acetylcholine.

NEUROTRANSMITTERS:

- **DOPAMINE:** Incr. alertness (incr. by cocaine). Also assoc. w/ pleasure/reward system in the brain (nucleus accumbens). Dopamine-blocking drugs (e.g. antipsychotics) cause drowsiness.
- **MELATONIN:** INHIBITED by light; therefore, incr at night. Initiates sleep. Part of our circadian rhythm. Explains why night shift workers can't sleep during the day.

Ascending Reticular Activating System



Most Common Sleep Disorders

- Obstructive Sleep Apnea
- Insomnia
- Restless Leg Syndrome
- Narcolepsy/ Hypersomnia

INSOMNIA

- Difficulty falling asleep (sleep latency), nocturnal awakenings, early awakening, poor quality and non-restorative. Also causes impairment during wake time.

TRANSIENT <1wk, at least 3 nights/wk

ACUTE < 1 mo.

CHRONIC > 1 mo.

OSA

- Diagnosed via sleep study in lab.
- **WORSENERD** by benzodiazepines, ETOH, opioids, anesthetics.
- **SUPPRESSED** by antidepressants, thryroxine, nicotine, progesterone.
- Blocked exhalation increases pulmonary pressure, which incr R ventricular pressure. Can lead to R sided LVH, then atrial fibrillation.

INSOMNIA:

PRIMARY or SECONDARY

- **PRIMARY**—more difficult to treat and often chronic.
- **SECONDARY**—most common. Time for detective work!

First look for environmental, behavioral or medical factors.

Secondary to **MANY** medical and psychiatric conditions.

Important Tx Principle:

- If the insomnia is secondary, try to treat the sleep and illness with the same medication first. E.g.: Bipolar disorder=sedating mood stabilizer, Depression=sedating antidepressant, Allergies=antihistamine, Pain=non-opioid pain treatments, etc.

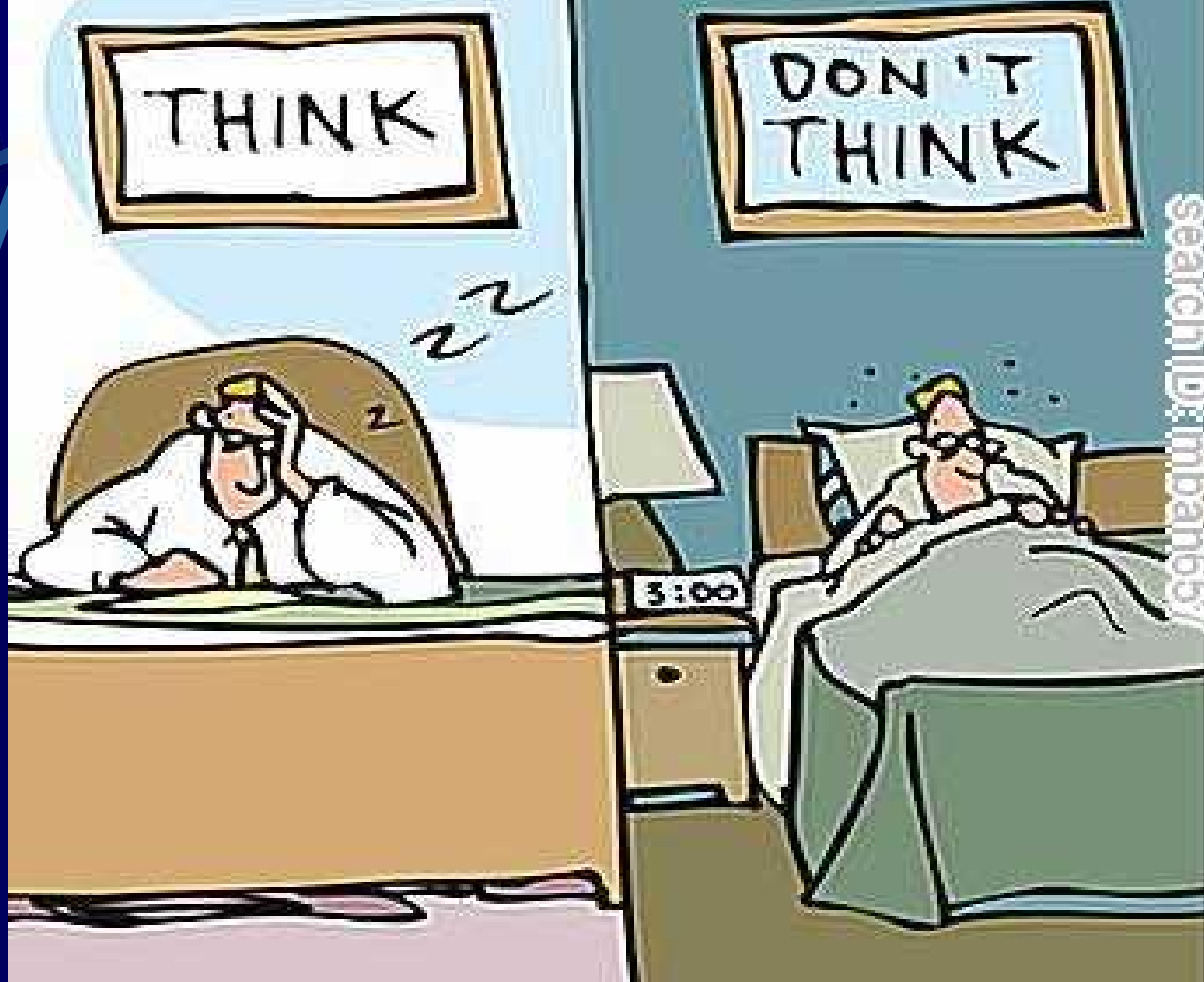
Psychiatric Causes of Disturbed Sleep

- **ANXIETY:** Often have delayed sleep latency or frequent awakening. Somnolent during the day and may take naps.
- **PANIC DISORDER:** Can have random panic attacks at night. Long acting benzodiazepine would benefit.
- **PTSD:** Incr nightmares, hypervigilance, restless sleep. Alpha blockers (eg clonidine, prazosin) showing benefit.

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Bipolar Disorder

- **MANIA:** Significantly less sleep needed per night or unable to sleep for days. Antidepressants (trazadone, doxepin, mirtazapine, etc) for sleep are contraindicated. Worsen mania. Sedating mood stabilizers work well.
- **DEPRESSION:** Atypical depression is more common. Mood stabilizers have shown most benefit. E.g. lamotrigine, lithium, aripiprazole, ziprasidone.

Depression

- Patients often have insomnia but can also have hypersomnia (associated with atypical depression).
 - Caution! Screen for bipolar d/o
 - Associated with early am waking
 - Treating the depression often corrects the sleep issues.
 - Try to treat both depression and sleep with an antidepressant.
 - Can concurrently tx with trazadone, mirtazapine, quetiapine, amitryptiline.

BORDERLINE PD



HYPERSOMNIAS

- Excessive daytime sleepiness or time spent sleeping. Tends to be secondary.
- Can be caused by diet, sleep hygiene, lack of exercise, substance abuse, thyroid, lifestyle, health, OSA, stimulant withdrawal, Kleine-Levin, encephalitis...long list!
- Attempt to treat with stimulating antidepressants if psychiatric. E.g.: bupropion, venlafaxine. Next step could be nuvigil / provigil, then stimulants as last resort.
- Possible existential problem.

NARCOLEPSY

- Sleep attacks—often with cataplexy.
- Associated w/ lucid dreaming, hypnogogic and hypnopompic hallucinations.
- Linked to $>$ HYPOCRETIN, which regulates sleep & appetite.
- Dx via sleep study and treated with stimulants.

HONORABLE MENTIONS:

- CIRCADIAN RHYTHM D/O
- DELAYED SLEEP PHASE SYNDROME
- SHIFT WORK
- FATAL FAMILIAL INSOMNIA

BIG MEDICAL WORDS

- SOMNILOQUY
- SOMNABOLISM
- SEXSOMNIA
- KLEINE-LEVIN SYNDROME
- PAVOR NOCTURNUS
- JACTATIO CAPITUS NOCTURNA

PARASOMNIAS

An undesirable phenomenon that occurs during sleep that causes distress & < function

SOMNABULISM=Sleep Walking.

PAVOR NOCTURNUS= Night Terrors

SOMLILOQUY= Sleep talking

NIGHTMARES—REM, more common in children. Affected by mood.

SLEEP PARALYSIS= Awake but can't move

BRUXISM--worsened by stimulants, antipsychotics and some antidepressants.

ENURESIS

SOMNABOLISM

- Occurs during N3.
- Begins around age 4, peaks age 12.
- >boys
- Person often unaware it occurred.
- Disoriented when awakened.
- Familial
- Requires safety precautions/ vigilance.
- Associated with zolpidem

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"I probably shouldn't wake him. He needs the exercise."

SLEEP TERRORS:

Often assoc. with sleep walking.

N3 stage

Person doesn't remember dream.

Not assoc. with stress.

No proven effective tx.

Possible benefit from benzo's.

More associated w/ children.

SLEEP HYGIENE:

1ST and most effective step.

- Keep a regular schedule. No naps.
- No nicotine, ETOH, caffeine, stimulants.
- Don't stay in bed if not able to sleep.
- No stimulating activities within 2hrs of bed.
- Relaxation, Meditation.
- Avoid lg. meal close to bedtime.
- A colder room, warm bath.

COGNITIVE BEHAVIORAL TREATMENT (CBT): CHANGE THOUGHTS AND BEHAVIOR THAT AFFECT SLEEP

- People usually get more sleep than they realize.
- Education about sleep and habits
- Do not associate the bed with insomnia or stress. Get out of bed if unable to sleep.
- Read something boring—suggest medical research journals.
- Do not perceive lack of sleep as a “disaster”. Can still get by.
- We have nothing to fear but the fear of insomnia itself!

LIGHT THERAPY:

- Better to do in AM
- Need light that provides 10K lux units.
- Most effective if cause is SAD.
- Exposure to light at least 30 minutes
- Can induce mania in bipolar patients.
- Light can adversely affect sleep by watching TV or computer before bed.

11 FDA-APPROVED HYPNOTICS:

NON-BENZODIAZEPINES: (affect GABA).

Meta-analysis showed superiority to benzo's for side effects.

ESZOPICLONE—Lunesta. Best for disrupted sleep. Long-acting. Duration~6-8hrs. Usually less hangover. Approved for long-term use.* My favorite to prescribe

ZOLPIDEM--Ambien. Best for sleep onset. Short action. Duration~4-6 hrs. Potential for dependence.

ZOLPIDEM ER--Ambien CR. Approved for long term use. Best for frequent awakening.

ZALEPLON—Sonata. Long acting. Indicated for short term use but showed efficacy for long-term.

11 FDA-APPROVED HYPNOTICS

BENZODIAZEPINES: Higher potential for tolerance, rebound, cognitive impairment, dependence, abuse, illegal sales, side effects and overdose. Affect sleep architecture. Avoid in elderly. Decr SWS

ESTAZOLAM--Prosom. 2-6 hr tx duration

FLURAZEPAM--Dalmane. Very long half-life. Up to 4 days!

QUAZEPAM—Doral. Selectively targets GABA-A for sleep. Rapid onset. Long-acting. $\frac{1}{2}$ life= 24hrs

TEMAZEPAM--Restoril. Duration 6-8 hrs.

TRIAZOLAM--Halcion. Rapid onset and short-acting. Best for sleep onset.

11 FDA-APPROVED HYPNOTICS:

TRICYCLICS: Affects sleep via H1 receptor

DOXEPIN—Sinequan, Silenor. Recommended for chronic insomnia and sleep maintenance.

MELATONIN AGONIST:

RAMELTEON--ROZERUM. Best for elderly. Reduced sleep onset by ~15-20 min and increased total sleep time by 40 min. Approved for long term use.

OFF-LABEL

- QUETIAPINE
- TRAZADONE
- GABAPENTIN
- AMITRYPTILINE
- THORAZINE
- VALERIAN ROOT
- MIRTAZAPINE

SWEET DREAMS

