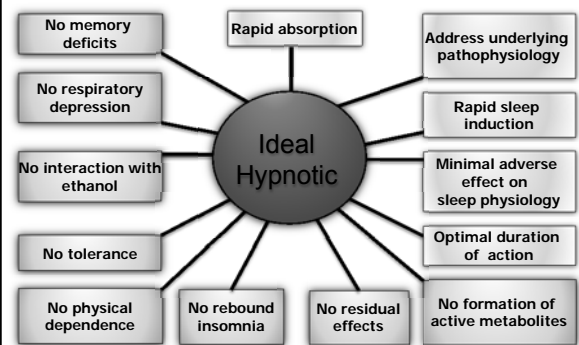


What Do People Take to Try to Improve Their Sleep?

Alcohol^{1,2,3}
Herbals^{3,4}
Dietary supplements^{1,4}
Homeopathic preparations⁴
Melatonin^{1,3,4}
OTC sleep aids²
Sedating antidepressants¹
Sedative-hypnotics^{1,5}
Melatonin receptor agonist
Hypocretin Receptor Antagonist

1. Neubauer DN. Clinical Cornerstone. 2003;5:16-27. 2. Ancoli-Israel S, Roth T. Sleep. 1999;22(suppl 2):S347-S353. 3. Wagner J et al. Neurosci Biobehav Rev. 2002;26:339-360. 4. Larzelere MM, Wiseman P. Prim Care Clin Office Pract. 2002;29:339-360. 5. Miller MM. Sleep. 2000;23(suppl 1):S39-S47.

Characteristics of the Ideal Hypnotic

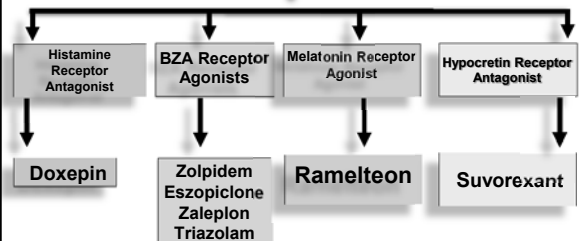


Adapted from Mendelson et al. Sleep Med Rev 2004;8:17.

What Do People Take to Try to Improve Their Sleep?

28% use alcohol

Drug classes



Sleep Diary

In bed at 7:45 PM
Asleep at 9:45 PM
Awake at 11:00 PM
~~Awake~~
Asleep at 11:30 PM
Awake at 4:00 AM
~~Awake~~
Asleep at 4:15 AM
Awake at 5:24 AM
~~Awake~~
Asleep at 5:35 AM
Awake at 8:00 AM

Hypnotics: Mechanism of Action & Labeling

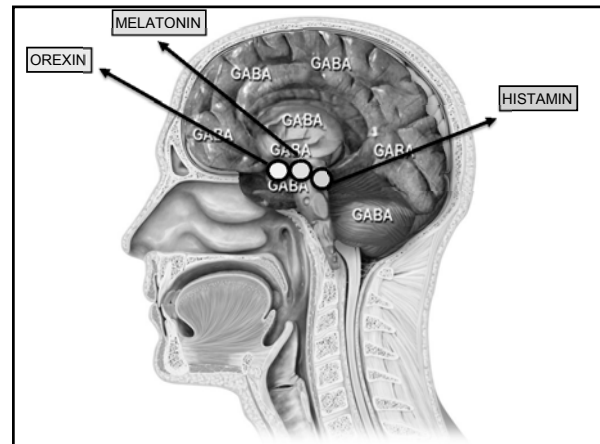
Class ¹	Drugs ^{1,2}	Acts on: ¹	Controlled Substance Schedule ²
Barbiturates	Phenobarbital, methobarbital, amobarbital, secobarbital	Non-selective CNS depressants	II, III, IV
Antipsychotics	Quetiapine, risperidone, ziprasidone	Dopamine, serotonin	Not scheduled
Antidepressants	Trazodone, amitriptyline	Serotonin/histamine	Not scheduled
Benzodiazepines	Temazepam, estazolam, flurazepam, quazepam, triazolam	GABA	IV
Antihistamines	Diphenhydramine ³	Histamine	Not scheduled
Nonbenzodiazepines	Zolpidem, eszopiclone, zaleplon	GABA	IV
Melatonin receptor agonist	Ramelteon	Melatonin	Not scheduled
Selective H ₁ receptor antagonist ⁴	Doxepin	Histamine H ₁	Not scheduled
Orexin receptor antagonist ⁴	Suvorexant	Orexin	IV

1. Roth T, Colepner L. Clinical Symposia. 2009;68:1-32. 2. Controlled Substances Act. <http://www.deadiversion.usdoj.gov/21cfr/cfr812.htm>. Accessed June 9, 2015. 3. SILENCIO® (doxepin) [package insert]. Morristown, NJ: Perrin Therapeutics; 2014. 4. Suvorexant® (suvorexant) [package insert]. Whitehouse Station, NJ: Merck and Co. 2014. 5. Richardson GS et al. J Clin Psychopharmacol. 2002;22:11-15.

DRUGS INDICATED FOR INSOMNIA

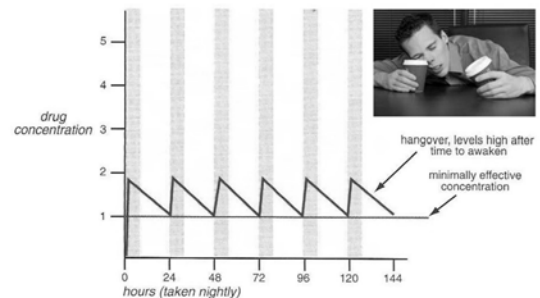
Generic	Brand	T _{1/2} (Hours)	Dose (mg)	Drug Class
Flurazepam	Dalmane	48-120	15-30	BZD
Temazepam	Restoril	8-20	15-30	BZD
Triazolam	Halcion	2-6	0.125-0.25	BZD
Estazolam	Prosom	8-24	1-2	BZD
Quazepam	Doral	48-120	7.5-15	BZD
Zolpidem	Ambien	1.5-2.4	5-10	non-BZD
Zaleplon	Sonata	1	5-20	non-BZD
Eszopiclone†	Lunesta	5-7	1-3	non-BZD
Zolpidem Ex Rel†	Ambien CR	1.5-2.4*	6.25-12.5	non-BZD
Ramelteon†	Rozerem	1.5-5	8	MT agonist
Silenor†	Doxepin	15.3	3, 6	H ₁ Antagonist
Suvorexant†	Belsomra	12	5, 10, 15, 20	Hcrt Antagonist

* Modified formulation. †No short-term use limitation.



Agent	Initiates Sleep	Maintains Sleep	Sleep with limited opportunity	Required Inactivity (hr)	Dose (mg)
Eszopiclone	✓	✓		8+	1,2,3
Zaleplon	✓		✓	4	5,10
Zolpidem	✓			7-8	5,10
Extended release	✓	✓		7-8	6.25, 12.5
Intermezzo (Sublingual)		✓	✓ (4 hrs)	4	1.75, 3.5
Zolpimist (oral spray)	✓			4	5, 10
Elduar (Sublingual)	✓			4	5, 10
Silenor		✓		7-8	3, 6
Ramelteon	✓			-	8
Suvorexant	✓	✓		7	5, 10, 15, 20

Moderately Long Half-Life Hypnotics Do Not Wear off Until After Time to Awaken (Hangover)

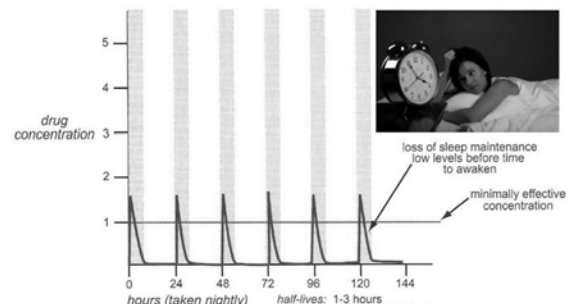


Stahl (2008). *Essential Psychopharmacology*, p. 835.

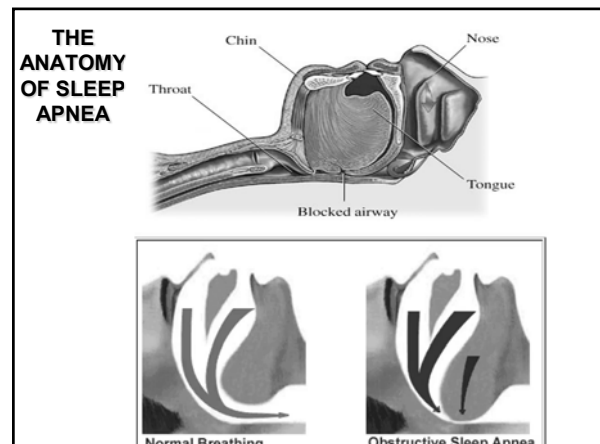
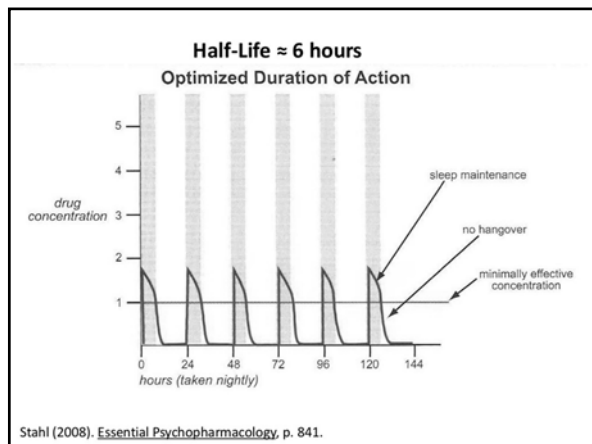
BZRA Hypnotics: Possible Adverse Effects



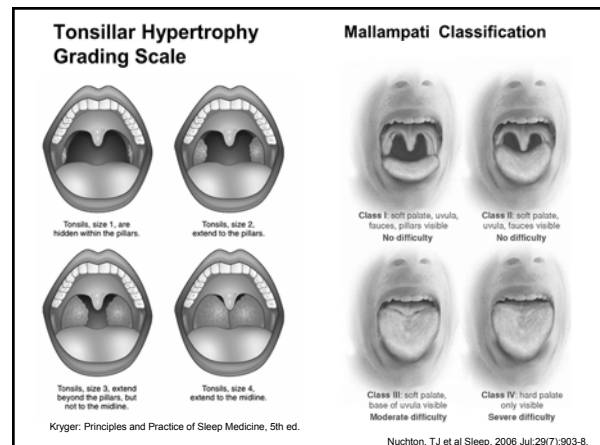
Ultrashort Half-Life Hypnotics Wear off Before Time to Awaken (Loss of Sleep Maintenance)



Stahl (2008). *Essential Psychopharmacology*, p. 840.



OBSTRUCTIVE SLEEP APNEA SYNDROME



Treatment of OSA

NON-SURGICAL

- Weight loss
- CPAP/BiPAP
- Positional Tx
- Oral Appliances
- Drugs
- Avoidance of Rx/Etoh

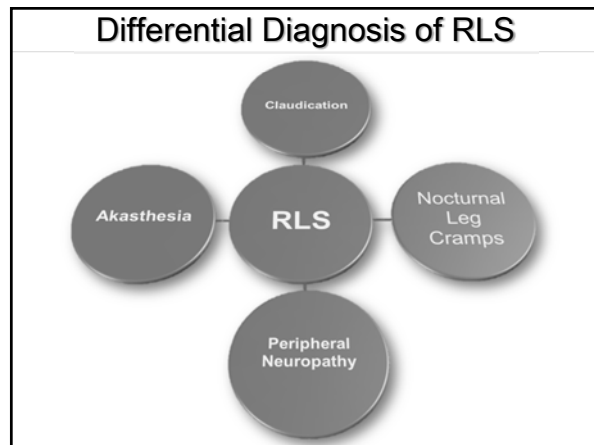
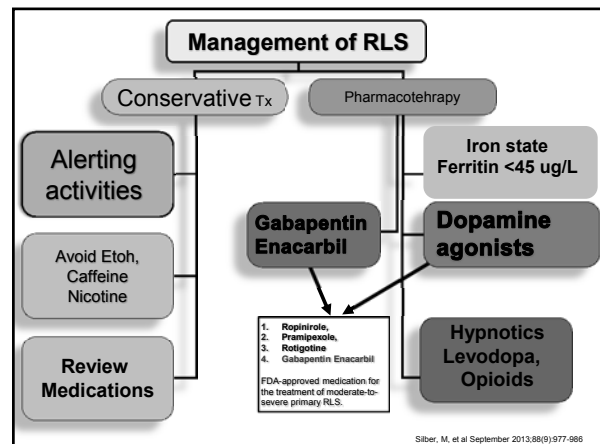
SURGICAL

- UPPP
- LAUP
- Bimax Advancement
- Trach

Before

After

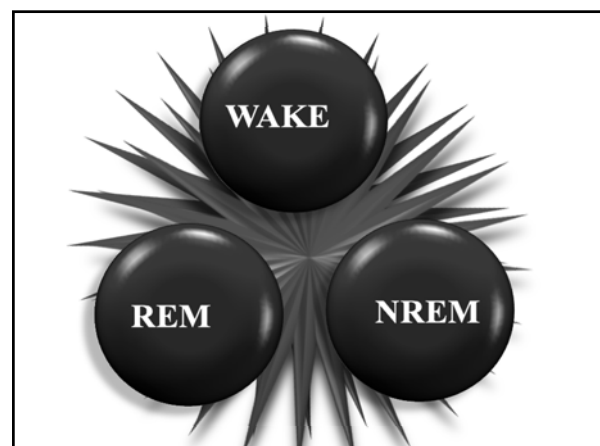
Willis-Ekbom Disease	
Essential Criteria*	Supportive Features*
<div><div></div><div>Urges to move the legs — usually accompanied or caused by uncomfortable leg sensations</div></div>	<div><div>— Sleep disturbances</div><div>— Periodic leg movements</div><div>— Positive family history for RLS</div><div>— Positive response to dopaminergic therapy</div></div>
<div><div></div><div>Getting up: Temporary relief with movement — partial or total relief from discomfort by walking or stretching</div></div>	
<div><div></div><div>Rest: Onset or worsening of symptoms at rest or inactivity, such as when lying or sitting</div></div>	
<div><div></div><div>Evening: Worsening or onset of symptoms in the evening or at night</div></div>	
<div><div>*</div><div>Diagnostic criteria developed by the International RLS (RLS) Study Group in collaboration with the National Institutes of Health (NIH).</div></div>	
<div><div>Allen et al. Sleep Med. 2003;4:101-119.</div></div>	



Narcolepsy

- Disorder of unknown etiology
- Consists of:
 - Excessive sleepiness
 - REM sleep phenomena (i.e cataplexy)

RLS	PLMS
<ul style="list-style-type: none"> ✓ RLS is a symptom based Dx ✓ RLS is Dx in the physician's office ✓ 80% of people who have RLS will have PLM's 	<ul style="list-style-type: none"> ✓ PLMS are an EMG finding ✓ PLM's are Dx in the sleep lab ✓ 30% of individuals who have PLM's have RLS symptoms



Case

- A 64 y/o man presented to the ER with a broken wrist experienced during a “fighting dream.” For the last 6m, he has been sleeping in a separate room than his wife after he had punched her during one of these dreams. What is the most likely diagnosis?

Summary: Treatments of Sleep Disorders

Condition	Nonpharmacologic	Pharmacologic
Insufficient Sleep Syndrome	Increase total sleep time, e.g., naps	Not recommended
Obstructive Sleep Apnea	Positive Pressure Therapy Airway surgery (CPAP)	Modafinil* (for residual sleepiness with CPAP compliance)
Insomnia	Behavioral Tx	BZA*, non-BZA agonists*, H1 antidepressants*, melatonin agonist, Hcrt antagonist*
Narcolepsy	Prophylactic “power naps”	Modafinil*, dexamphetamine*, methylphenidate*
RLS	Hot bath, massage	Dopaminergic agents, Dopamine agonist*, $\alpha 2$ delta ligand.
Parasomnias	Safety, Avoid exacerbating factors	BZA

REM Sleep Behavior Disorder

RBD is most commonly associated with neurodegenerative disease, particularly α -Synucleinopathies:

- Parkinson’s disease
- Dementia with Lewy Bodies
- Multiple System Atrophy

Pharmacologic treatment of RBD

Drug (*)	Dose	Level of Recommendation	Special considerations
Environmental Safety			
Clonazepam	0.25-2.0 mg QHS	Suggested (*)	Use with caution in patients with dementia, gait disorders, or concomitant OSA. Side effect include sedation, impotence, motor incoordination, confusion and memory dysfunction.
Melatonin	3 mg to 12 mg before bedtime.	Suggested(*)	Effective in patients with alpha-synucleinopathies, memory problems, and sleep-disordered breathing. Side effects include headaches, sleepiness and delusions/hallucinations.