Sleep and Pain
What is a good night’s sleep?
Normal Sleep

- Quantity – 7-8 hours for most people
- Quality – restful, awaken refreshed
Sleep Architecture
<table>
<thead>
<tr>
<th>TYPE OF SLEEP</th>
<th>STAGE OF SLEEP</th>
</tr>
</thead>
<tbody>
<tr>
<td>NREM:</td>
<td></td>
</tr>
<tr>
<td>NREM sleep contributes to physical rest and may bolster the immune system.</td>
<td>Stage 1 (Light Sleep): A transitional stage between waking and sleeping, usually lasting 5 or 10 minutes. Breathing becomes slow and regular, the heart rate decreases, and the eyes exhibit slow rolling movements.</td>
</tr>
<tr>
<td>Researchers often group NREM stages 3 and 4 together, calling them delta sleep.</td>
<td>Stage 2 (True Sleep): A deeper stage of sleep where fragmented thoughts and images pass through the mind. Eye movements usually disappear, muscles relax, and there is very little body movement.</td>
</tr>
<tr>
<td></td>
<td>Stage 3 (Deep Sleep): A further deepening of sleep with additional slowing of heart and breathing rates.</td>
</tr>
<tr>
<td></td>
<td>Stage 4 (Deep Sleep): This is the deepest stage of sleep, in which arousal is the most difficult. Typically, sleep walking and bed-wetting occur in this stage.</td>
</tr>
</tbody>
</table>
REM Sleep:
REM sleep contributes to psychological rest and long-term emotional well-being. It may also bolster memory.

REM Stage (Dream Sleep):
A dramatic decrease in muscle tone and an essential paralysis characterize this stage of sleep. Other characteristics are irregular breathing, increased heart rate, and rapid eye movements. The brain's oxygen consumption increases, and temperature regulatory mechanisms are absent. In this stage, people experience vivid, active dreams with complex symbols.
How is Sleep Related to Pain?
1. Poor tissue repair
2. Poor filtering

Poor Sleep

Increased Pain

Alpha Intrusion
Pain Interferes with Normal Sleep

- Alpha wave intrusion on sleep – deep, delta wave sleep is disrupted

- The alpha-EEG anomaly is... [seen] for patients with FM and it has been described in patients with RA, osteoarthritis and primary Sjogren's syndrome. The anomaly has also been described in patients without rheumatic disorders, such as in various psychiatric diseases, post-infectious and post-traumatic patients with fatigue and pain, and patients suffering from the chronic fatigue syndrome.

Poor Sleep Increases Pain

- Pain severity was related to fewer hours slept and delayed sleep onset.
  

- Low levels of somatomedin C in patients with the fibromyalgia syndrome. A possible link between sleep and muscle pain.
  

- Sleep deprivation lowers the pain threshold – bypasses the “Caller ID”
Sleep in Fibromyalgia

- Poorer sleepers tended to report significantly more pain. A night of poorer sleep was followed by a significantly more painful day, and a more painful day was followed by a night of poorer sleep.

- Sequential daily relations of sleep, pain intensity, and attention to pain among women with fibromyalgia Pain. 1996 Dec;68(2-3):363-8.

- Lower concentrations of tryptophan and metabolites have been found in the cerebrospinal fluid of patients with FM

- Lower levels of IGF-1 have been found in people with FM (related to low growth hormone), which depends on stage 3 + 4 sleep for its production
Within a year: 30% of people

At any one time:
- 10% chronic insomnia
- 15% short-term insomnia
- 50% is psychological
People buy more over-the-counter and prescription sleeping medications than any other drug.

CBS Healthwatch
How Can you Improve Sleep?
Remove the peas
The Rules of Tacks

- If you are sitting on a tack, it takes a lot of aspirin to make the pain go away.
- If you are sitting on 2 tacks, removing one does not lead to a 50% improvement in symptoms.

-Sid Baker, M.D.
Causes

- Exogenous – Outside World
- Physical – Your Body
- CNS – Your nervous system
- Psychological
  - Sleep state Misperception
Causes - Exogenous

- External stimuli:
  - Noise
  - Excessive heat or cold
  - Bright light
  - Partner with snoring or restless legs
  - Pets

Stimulants
- Coffee
- Chocolate
- Tea

- Marijuana, alcohol

- Medications:
  - Sleeping pills and Tranquilizers ("rebound")
  - Thyroid preparations
  - Oral contraceptives
  - Beta-blockers
  - SSRI’s
Alcohol and Sleep

- Alcohol is more disruptive to sleep than caffeine
  - The body will produce adrenaline to compensate for the alcohol in the system
  - Alcohol makes people thirsty
Causes - Physical

- Bodily dysfunctions:
  - Pain.
  - Decreased mobility.
  - Disturbing sensations or movements
    - Periodic limb movements – see next slide
  - Cardiac or respiratory problems
    - Asthma
    - Heart failure
  - Sleep apnea
  - GI – reflux, IBD
  - Age.
Periodic Limb Movements, “Restless Legs”

- Familial – consider megadoses of folic acid
  - 10-30 mg per day
- Check iron – iron deficiency may also provoke
- For nocturnal myoclonus:
  - Magnesium
  - Vitamin E
  - Parkinson’s Drugs
Sleep Apnea

- Snoring
- Daytime Sleepiness
- Hypertension
- Car accidents
- Heart Failure
- Stroke
- Arrhythmia
- Etc.
Causes - CNS

- Alterations in the central nervous system (CNS) that initiate and maintain sleep.
  - Brain: stroke, head injury, dementia.
  - Metabolic: liver disease, blood sugar, etc.
    - For repetitive 3 am awakening, try a protein snack before bed.
  - Hormonal: thyroid, menopause.
Causes - Psychological

- Personality:
  - Anxious, tense, somatic vs.
  - Relaxed, phlegmatic.
- Stress.
  - Life changes (birth, death, divorce, move, etc.).
- Depression
- Circadian rhythm sleep disorder
- Poor Sleep Hygiene
The Vicious Cycles

- Insomnia
- Performance
- Anxiety
- Negative Conditioning
- Secondary Gain
Differentiating Causes

- Difficulty falling asleep
  - Poor sleep hygiene
  - Conditioned insomnia (behavioral conditioning)
  - Restless legs syndrome
  - Circadian rhythm disorder
  - Advanced sleep-phase syndrome
  - Delayed sleep-phase syndrome

- Difficulty staying asleep
  - Medications
  - Drug or alcohol use
  - Psychiatric disorders (e.g. Depression, anxiety)
  - Medical disorders
  - Sleep-disordered breathing (e.g., Sleep apnea)
  - Nocturnal myoclonus
Solutions

- Remove causal factors
- Behavioral changes –
  - Sleep hygiene
  - Sleep restriction therapy
  - Stimulus control therapy
  - Relaxation techniques
- Herbs and Medications
Remove Causal Factors

- Stop alcohol, stimulants, etc
- Treat pain
- Treat heart failure, sleep apnea, etc
- Earplugs/ heavy curtains, etc
- Treat partner
Solutions

- Remove causal factors
- Behavioral changes –
  - Sleep hygiene
  - Sleep restriction therapy
  - Stimulus control therapy
  - Relaxation techniques
- Herbs and Medications
Principles of Sleep Hygiene

- Go to bed and get up at the same time each day
- Avoid daytime naps or limit them to one midafternoon nap
- Avoid evening alcohol use
- Avoid caffeinated drinks (late in the day)
Sleep Hygiene Continued

- Reduce or eliminate tobacco use, especially at night or in the evening

- Exercise in moderation; avoid evening exercise

- Use the bed only for sleep and sexual activity
Sleep Hygiene Continued

- Keep the bedroom dark, quiet, and cool
- Avoid stress and worrisome thoughts in the evening before sleep
- Avoid screen time or bright light for an hour before bed
Light Therapy

- Bright light in the morning
- Avoidance of bright light in the evening
- This works even in alcohol withdrawal
Stimulus Control Therapy

- Associate bed, sleep environment only with sleep, intimacy
- No reading, eating, or watching TV in bed.
- Get out of bed and do something relaxing if unable to sleep after 15 to 20 minutes.
  (Not TV – light and content are arousing)
Solutions

- Remove causal factors
- Behavioral changes –
  - Sleep hygiene
  - Sleep restriction therapy
  - Stimulus control therapy
  - Relaxation techniques
- Herbs and Medications
Sleep Restriction Therapy

- No Naps
- Rise at same time regardless of how little sleep
- Limit sleep to 1-2 hours less than reported amount of sleep
  - Makes sleep more continuous
- Then gradually increase sleep time
Solutions

- Remove causal factors
- Behavioral changes –
  - Sleep hygiene
  - Sleep restriction therapy
  - Stimulus control therapy
  - Relaxation techniques
- Herbs and Medications
Relaxation techniques

- Mental
  - Prayer
  - Journal
  - Imagery
  - Biofeedback
  - Delta wave inducing sleep CD
  - Music – postoperative study in CABG patients

- Physical
  - Breathing
  - Progressive Relaxation
  - Sounder Sleep System
Non-Drug Therapies Really Do Work!

- Behavioral management of sleep disturbances secondary to chronic pain.


Documented effectiveness of a behavioral program on EEG and sleep architecture in patients with chronic pain.
The Sounder Sleep Solution

Based on a program developed by Michael Krugman

www.soundersleep.com
Solutions

- Remove causal factors
- Behavioral changes –
  - Sleep hygiene
  - Sleep restriction therapy
  - Stimulus control therapy
  - Relaxation techniques
- Herbs and Medications
Pills and Potions

Herbs and Medications to Aid Sleep
Medications – Pros and Cons

**Pros**
- Work quickly
- Covered by insurance

**Cons**
- Stop working (Tolerance)
- Dependence – Rebound
- Sedation
  - Fall Risk
  - Confusion
- Amnesia
Natural Substances

- Minerals
  - Calcium and Magnesium
- Amino Acids: Tryptophan, 5HTP
- Hormones: Melatonin
- Herbs
- Aromatherapy
Serothonin

- Neurotransmitter in the brain that triggers sleep
- Made from tryptophan – amino acid found in foods such as milk, turkey
5HTP

- Increase REM sleep (typically by about 25%)
- Increase deep sleep stages 3 and 4
- No increase in total sleep time

- 100–300 mg 30–45 minutes before retiring
Melatonin

- Hormone produced by the pineal gland – part of the system that aligns our body with light and dark
  - Dosage: 3 mg at bedtime is more than enough
  - Dosages as low as 0.1 and 0.3 mg have been shown to produce a sedative effect when melatonin levels are low

- Caution: Could disrupt the normal circadian rhythm. In one study, a daily dosage of 8 mg/day for only 4 days resulted in significant alterations in hormone secretions
Passionflower

- The herbal “specific” for staying asleep
- Studied vs. serax (benzodiazepine) for anxiety:
  - Equally effective for anxiety
  - No cognitive or motor impairment
Valerian

- Takes 2 – 3 weeks to start working
- Shown to significantly
  - reduce sleep latency
  - improve sleep quality
  - reduce night-time awakenings
- Usually reduces morning sleepiness.
Valerian

- Studies:
  - Compared with placebo, valerian showed a significant effect
    - 44% reporting perfect sleep
    - 89% reporting improved sleep.
Valerian

Studies:

Double-blind study of insomniacs:

- Valerian root extract (160 mg) and Melissa officinalis extract (80 mg)
- Benzodiazepine (triazolam 0.125 mg)
- Placebo.

Results:

- Valerian effect comparable to drug
- Able to increase deep sleep stages 3 and 4.
- Did not cause daytime sedation
  - No evidence of diminished concentration based on the Concentration Performance Test
  - No impairment of physical performance
Other Herbs Used Traditionally

- Lemon Balm
- Hops
- Chamomile
- Skullcap
- Kava – cautions for the liver
- End Fatigue Revitalizing Sleep Formula
Aromatherapy

- Essential oil – scent or in hydrotherapy
  - Lavender – nursing home study
  - Rose
  - Ylang-ylang
  - Neroli
Drugs
The Ideal Sleeping Pill

- Shorten latency to sleep
- Maintain normal physiological sleep all night without blocking normal behavioral responses to the crying baby or the alarm clock
- Leave neither hangover nor withdrawal effects the next day
- No tolerance or side effects, such as impairment of breathing, cognition, ambulation, and coordination
- Not habit-forming or addicting.
The Ideal Sleeping Pill

- Has not been developed
Mortality according to Hypnotic Prescriptions

Confirmed for zolpidem, temazepam, lunesta, sedative antihistamines

Over-the-counter Drugs

- e.g. Nytol, Sleep-Eez, Sominex, Anacin PM, Excedrin PM, Tylenol PM, Unisom

- antihistamines
  - not addictive
  - not effective in sustaining stage IV sleep
  - can affect the quality of sleep.

- YOU SLEEP MORE, BUT IT IS WORSE SLEEP
Implications of Half-Life

![Graph showing blood level over time with half-life indicated.](image-url)
# Long vs. Short-Acting Hypnotics

<table>
<thead>
<tr>
<th></th>
<th>Short</th>
<th>Long</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hangover</strong></td>
<td>+</td>
<td>++++</td>
</tr>
<tr>
<td><strong>Accumulation</strong></td>
<td>0</td>
<td>+++</td>
</tr>
<tr>
<td><strong>Tolerance</strong></td>
<td>++++</td>
<td>+</td>
</tr>
<tr>
<td><strong>Withdrawal insomnia</strong></td>
<td>++++</td>
<td>+</td>
</tr>
<tr>
<td><strong>Decrease anxiety</strong></td>
<td>0</td>
<td>+++</td>
</tr>
<tr>
<td><strong>Amnesia</strong></td>
<td>++++</td>
<td>++</td>
</tr>
</tbody>
</table>
Table 1  -- Drugs with a Food and Drug Administration indication for insomnia

<table>
<thead>
<tr>
<th>Drug name</th>
<th>Mechanism of action</th>
<th>Dose range</th>
<th>Elimination half-life</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estazolam (ProSom)</td>
<td>BzRA</td>
<td>1–2 mg</td>
<td>10–24 h</td>
</tr>
<tr>
<td>Flurazepam (Dalmane)</td>
<td>BzRA</td>
<td>15–30 mg</td>
<td>48–120 h[^a]</td>
</tr>
<tr>
<td>Temazepam (Restoril)</td>
<td>BzRA</td>
<td>15–30 mg</td>
<td>8–20 h</td>
</tr>
<tr>
<td>Triazolam (Halcion)</td>
<td>BzRA</td>
<td>0.125–0.25 mg</td>
<td>2.4 h</td>
</tr>
<tr>
<td>Quazepam (Doral)</td>
<td>BzRA</td>
<td>7.5–15 mg</td>
<td>48–120 h[^a]</td>
</tr>
<tr>
<td>Zolpidem (Ambien)</td>
<td>BzRA</td>
<td>5–10 mg</td>
<td>1.4–3.8 h</td>
</tr>
<tr>
<td>Zolpidem ER</td>
<td>BzRA</td>
<td>6.25–12.5 mg</td>
<td>2.8 h</td>
</tr>
<tr>
<td>Zaleplon (Sonata)</td>
<td>BzRA</td>
<td>5–20 mg</td>
<td>1 h</td>
</tr>
<tr>
<td>Eszopiclone (Lunesta)</td>
<td>BzRA</td>
<td>1–3 mg</td>
<td>6 h</td>
</tr>
<tr>
<td>Ramelteon (Rozerem)</td>
<td>MtRA</td>
<td>8 mg</td>
<td>1–2.6 h</td>
</tr>
<tr>
<td>Name</td>
<td>Dose (mg)</td>
<td>Absorption</td>
<td>Active Metabolite</td>
</tr>
<tr>
<td>-------------------------------</td>
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<td>---------------------</td>
<td>-------------------</td>
</tr>
<tr>
<td>Chlordiazepoxide (Librium)</td>
<td>5-10</td>
<td>Intermediate</td>
<td>Yes</td>
</tr>
<tr>
<td>Diazepam (Valium)</td>
<td>2-10</td>
<td>Fast</td>
<td>Yes</td>
</tr>
<tr>
<td>Estazolam (ProSom)</td>
<td>0.5-2.0</td>
<td>Intermediate</td>
<td>Yes</td>
</tr>
<tr>
<td>Flurazepam (Dalmane)</td>
<td>7.5-30</td>
<td>Intermediate to fast</td>
<td>Yes</td>
</tr>
<tr>
<td>Clorazepate (Tranxene)</td>
<td>7.5-15</td>
<td>Fast</td>
<td>Yes</td>
</tr>
<tr>
<td>Clonazepam (Klonopin)</td>
<td>0.5-1.0</td>
<td>Intermediate</td>
<td>Yes</td>
</tr>
<tr>
<td>Quazepam (Doral)</td>
<td>7.5-15</td>
<td>Intermediate</td>
<td>Yes</td>
</tr>
<tr>
<td>Oxazepam (Serax)</td>
<td>10-15</td>
<td>Slow</td>
<td>No</td>
</tr>
<tr>
<td>Lorazepam (Ativan)</td>
<td>0.5-4.0</td>
<td>Intermediate</td>
<td>No</td>
</tr>
<tr>
<td>Temazepam (Restoril)</td>
<td>7.5-15</td>
<td>Slow</td>
<td>No</td>
</tr>
<tr>
<td>Alprazolam (Xanax)</td>
<td>0.25-2</td>
<td>Intermediate</td>
<td>No</td>
</tr>
<tr>
<td>Triazolam (Halcion)</td>
<td>0.125-0.5</td>
<td>Intermediate</td>
<td>No</td>
</tr>
<tr>
<td>Midazolam (Versed)</td>
<td>7.5-15</td>
<td>Intermediate</td>
<td>No</td>
</tr>
<tr>
<td>Zolpidem (Ambien)</td>
<td>5-10</td>
<td>Intermediate</td>
<td>No</td>
</tr>
<tr>
<td>Medications Used for Insomnia</td>
<td></td>
<td></td>
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<tr>
<td>-------------------------------</td>
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</tr>
<tr>
<td><strong>Imidazopyridines</strong>&lt;br&gt;Selective for alpha-1 GABA R</td>
<td>Zolpidem (Ambien) 5-10 mg&lt;br&gt;Zaleplon (Sonata) 5-10 mg</td>
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<tr>
<td><strong>Less selective GABA R agonist</strong></td>
<td>Eszopiclone (Lunesta) 2-3 mg</td>
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<tr>
<td><strong>Melatonin receptor agonist</strong></td>
<td>Rozerem 8 mg</td>
<td></td>
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<tr>
<td><strong>Antihistamines</strong></td>
<td>Diphenhydramine (Benadryl) 25 – 50 mg</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Sedating antidepressants</strong></td>
<td>Amitriptyline (Elavil) 10–75mg&lt;br&gt;Trazodone (Desyrel) 25–100mg&lt;br&gt;Doxepin 10 – 75 mg&lt;br&gt;Imipramine 25 – 100 mg&lt;br&gt;Remeron 15 mg</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Anticonvulsants</strong></td>
<td>Neurontin 300 – 1500 mg&lt;br&gt;Helps pain and PLM/Restless legs&lt;br&gt;Gabitril 4 mg 1-3 at bedtime</td>
<td></td>
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</tr>
<tr>
<td><strong>Muscle relaxants</strong></td>
<td>Soma 350 mg&lt;br&gt;Addictive&lt;br&gt;Flexeril 10 – 20 mg at bedtime</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Other</strong></td>
<td>GHB (Xyrem)</td>
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<tr>
<td>Drug</td>
<td>Trade Name</td>
<td>Continuity</td>
<td>SWS</td>
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<tr>
<td><strong>TCAs</strong></td>
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<tr>
<td>Amitriptyline</td>
<td>Elavil</td>
<td>I (3)</td>
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<td>Doxepin</td>
<td>Sinequan</td>
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<td>Tofranil</td>
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<td>Nortriptyline</td>
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<td>I (1)</td>
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<td>Desipramine</td>
<td>Norpramin</td>
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<tr>
<td>Clomipramine</td>
<td>Anafranil</td>
<td>I (0–1)</td>
<td>I (1)</td>
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<td><strong>MAOIs</strong></td>
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<tr>
<td>Phenelzine</td>
<td>Nardil</td>
<td>D (1)</td>
<td>(0)</td>
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<tr>
<td>Tranylcypromine</td>
<td>Parnate</td>
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<td><strong>SSRIs</strong></td>
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<tr>
<td>Fluoxetine</td>
<td>Prozac</td>
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<td>Paroxetine</td>
<td>Paxil</td>
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<td>D (0–1)</td>
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<td>Sertraline</td>
<td>Zoloft</td>
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<td>Citalopram</td>
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<td>Fluvoxamine</td>
<td>Luvox</td>
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<tr>
<td>Escitalopram</td>
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<tr>
<td><strong>Other</strong></td>
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<tr>
<td>Bupropion</td>
<td>Wellbutrin</td>
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<td>Venlafaxine</td>
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<td>D (1)</td>
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<tr>
<td>Trazodone</td>
<td>Desyrel</td>
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<td>I (0–1)</td>
</tr>
<tr>
<td>Mirtazapine</td>
<td>Remeron</td>
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<td>I (2)</td>
</tr>
<tr>
<td>Nefazodone</td>
<td>Serzone</td>
<td>I (1)</td>
<td>(0)</td>
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</tbody>
</table>