



**Sleep Disorders and  
Developmental Disabilities**

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**Do you really want to sleep  
like a baby?**

**“He/She won’t sleep”**

**What goes through your mind  
when you hear this??**

**Your life is reflected in your sleep**



**Your sleep is a reflection of  
your life**

## Common Sleep Disorders

- Normal Sleep?
- Behavioral Insomnia of Childhood
- OSA/SDB
- Parasomnias
- PLM/RLS
- Narcolepsy
- Delayed Sleep Phase Syndrome

## Sleep History: 4 Elements

Amount  
Quality  
Timing  
State of Mind



Do you remember being tucked in?



## How do we get a child to sleep in the lab?



## No Need



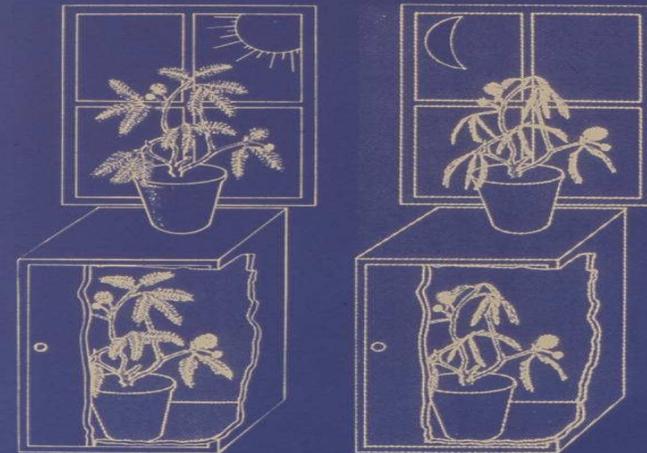
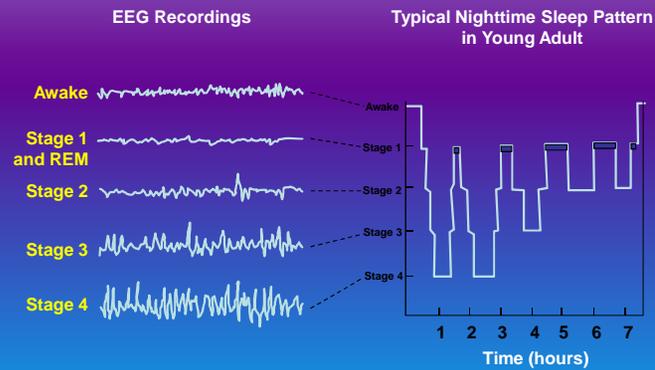
## Amount: Sleep Homeostasis



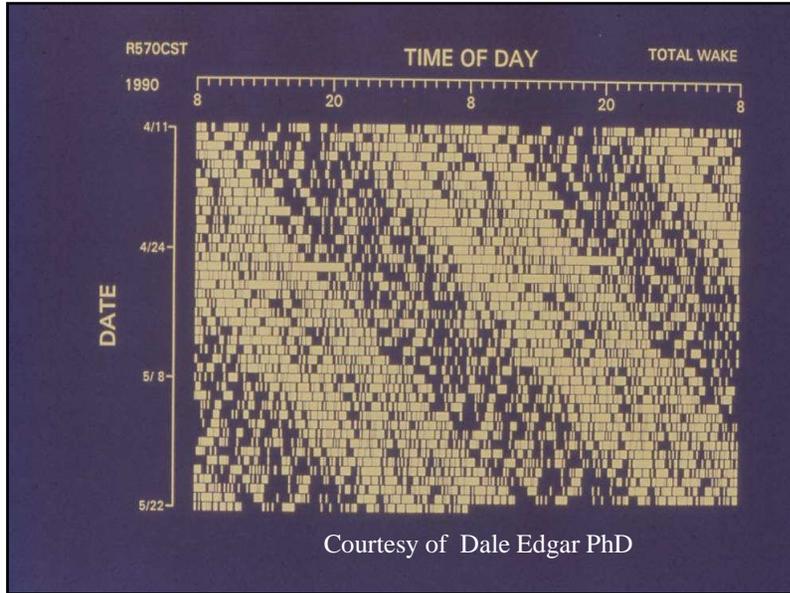
The power of sleep

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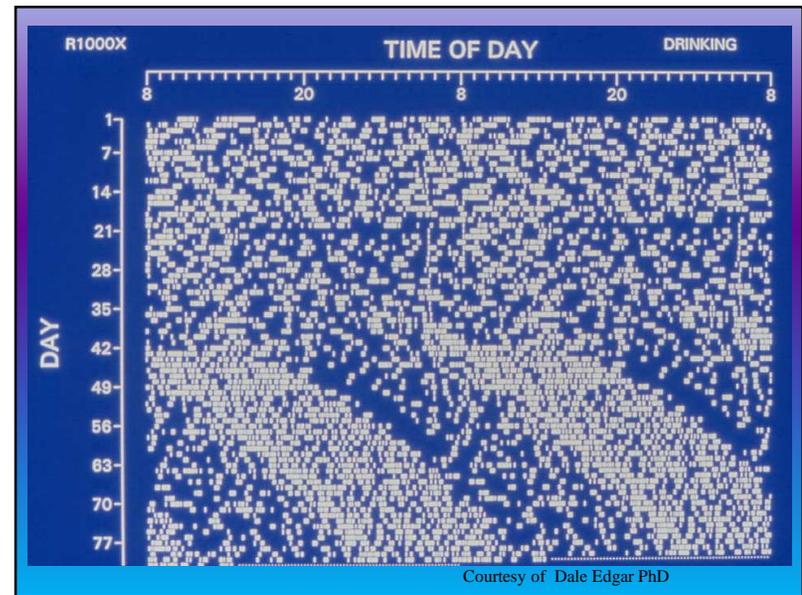
## Sleep Quality: Sleep Stages

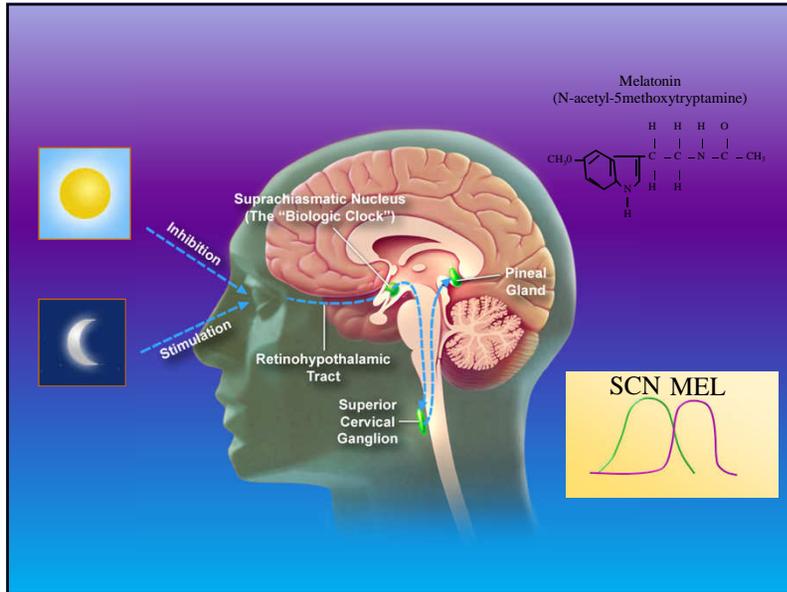


Courtesy of Dale Edgar PhD



**14.5 The Retinohypothalamic Pathway in Mammals** (a) This pathway carries information about the light-dark cycle in the environment to the SCN. For clarity of synaptic connections, the SCN is shown proportionately larger than other features. (b) Axons (seen at the bottom of the image) from the left eye are labeled red, while those from the right are green. Both eyes project so diffusely to the two overlying SCN that they are outlined in yellow. (Photograph courtesy of Cynthia L. Jordan.)



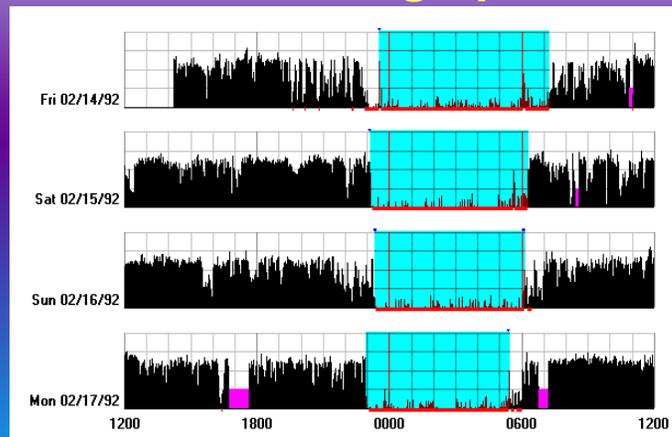


## Sleep Timing



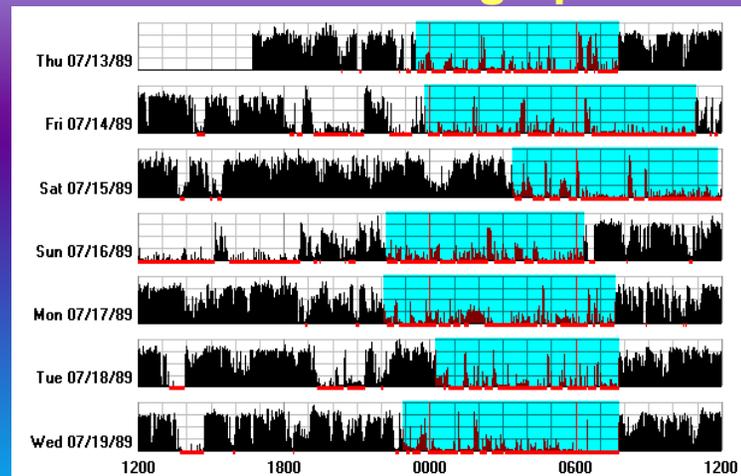
- Sleep timing is influenced by homeostatic and circadian factors
- The less we sleep the more sleep we need and vice versa
- Twice a day our alertness level peaks
- Twice a day our sleepiness peaks

## Normal Actigraph



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## Abnormal Actigraph



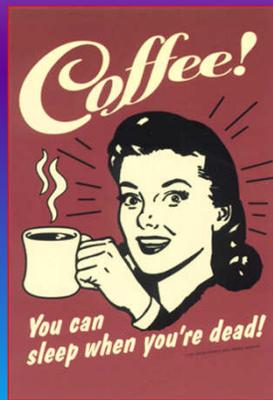
**The need for sleep is biological**  
**The way you sleep is learned**

What wakes you up may not be what keeps you awake

**What is the motivation to go to bed?**

**What is the motivation to get out of bed?**

**Kids and Sleep: What Are They On?**



**Trends in medication prescribing for pediatric sleep difficulties in US outpatient settings '07**

- Cross-sectional study on pts  $\leq 17$  yrs from '93-'04 NAMCS.
- 18.6 million visits occurred for sleep related difficulty in children most 6-12 yr.
- 81% of visits Rx'ed a med (only 48% of the adult patients with insomnia Rx'ed!)
- ... physicians frequently prescribed medications for sleep difficulties in children in US outpatient settings. Of particular concern is prescribing of many unapproved medications for this population

### The use of exogenous melatonin in delayed sleep phase disorder: a meta-analysis 2010

- Meta-analysis of RCT of melatonin in advancing DSPS pts
- 5 trials including 91 adults and 4 trials including 226 children showed that melatonin (0.3 -6 mg) advanced mean endogenous melatonin onset by 1.18 hours (0.89-1.48 h) and clock hour of sleep onset by 0.67 hours ( 0.45-0.89 h). Melatonin decreased sleep-onset latency by 23.27 minutes (4.83 -41.72 min). The wake-up time and total sleep time did not change significantly

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### Potential Pharmacokinetic Basis for Zolpidem Dosing in Children With Sleep Difficulties '07

- Open-label, dose-escalation study in children with insomnia. 21 children, seven per age group (2-6, >6 to 12, >12 to 18 years), received a single dose of zolpidem at one of the three dose levels (0.125, 0.25, or 0.50 mg/kg (20 mg maximum dose))
- Overall, zolpidem was well tolerated and a pediatric dose of 0.25 mg/kg is recommended for future efficacy studies



Do not to equate sedation with normal sleep!



### Paradoxical Reaction To A Hypnotic Medication



The real issue is not the pill but the  
 insomnia  
 The thought of sleeping wakes them  
 up

## SELF Correction

- Social
- Exercise
- Light
- Food

Sleeping should be silent

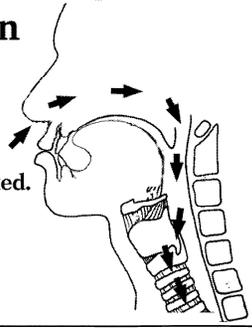


“...and on the box sat a fat and red-faced boy, in the state of somnolency.” C. Dickens

## Sleep Disorders in Children

### Correct Physiological Rest Position

Anterior portion of tongue on palate.  
Lips closed and relaxed.  
Teeth apart.  
Nasal breathing.

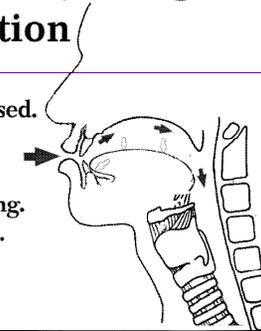


Naso-Respiratory Function and Cranialfacial Growth  
James McNamara 1979 as presented by James B. DuHammel DDS

## Sleep Disorders in Children

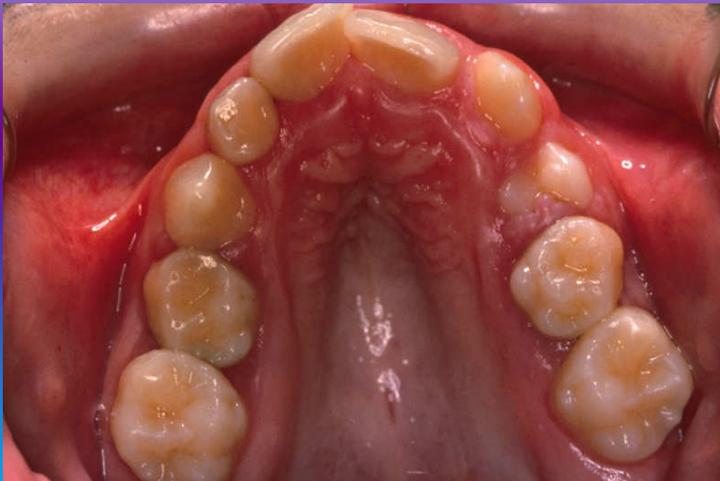
### Incorrect Physiological Rest Position

Tongue depressed.  
Lips apart.  
Teeth apart.  
Mouth breathing.  
Head forward.



Naso-Respiratory Function and Cranialfacial Growth  
James McNamara 1979 as presented by James B. DuHammel DDS

Thin people can have OSA too



## CPAP ain't just CPAP no more

- CPAP
- CPAP with C-Flex™/ EPR
- Bi-level
- Bi-level with Bi-Flex™
- Bi-level with a backup rate
- Automated CPAP
- Automated Bi-level
- Adaptive Servo Ventilator (SV) PAP

## OSA Treatments

- PAP: autoPAP, Bi-level, autoBi-Level, ASV, AVAPS, Bi-level ST, PAP for COPD
- Surgery: Maxilomandibular advancement and expansion, nasal valves and turbinates, pharyngoplasty, genioglossus advancement, Uvulopalatal flap
- Oral appliances: dozens available
- Conservative: Weight loss, positional therapy, weight loss
- Novel treatments: Winx and Provent
- Experimental options: Hypoglossal stimulators

## CPAP



## Can Sleepy Students Learn Anything?



## School Start Times for Adolescents AAP 2014

Insufficient sleep in adolescents as an important public health issue...the evidence strongly implicates earlier school start times (ie, before 8:30 am) as a key modifiable contributor to insufficient sleep...research has now demonstrated that delaying school start times is an effective countermeasure to chronic sleep loss. The AAP strongly supports the efforts of school districts to optimize sleep in students and urges high schools and middle schools to aim for start times that allow students the opportunity to achieve optimal levels of sleep (8.5–9.5 hours)

## Sleep impacts behavior



## Sleep disorders mimic attention and learning disorders

## Slumber Parties ain't about sleeping



Any Questions?

### National Institutes Of Health State-of-the-Science Manifestations And Management Of Chronic Insomnia In Adults June'05

Chronic insomnia is a major public health problem affecting millions of individuals, along with their families and communities. Little is known about the mechanisms, causes, clinical course, comorbidities, and consequences of chronic insomnia. Evidence supports the efficacy of cognitive-behavioral therapy and benzodiazepine receptor agonists in the treatment of this disorder. Very little evidence supports the efficacy of other treatments, despite their widespread use. Moreover, even for those treatments that have been systematically evaluated, the panel is concerned about the mismatch between the potential lifelong nature of this illness and the longest clinical trials, which have lasted 1 year or less. A substantial public and private research effort is warranted, including the development of research tools and the conduct of longitudinal studies and randomized clinical trials. Finally, there is a major need for educational programs directed at physicians, health care providers, and the public.

## Benzodiazepine hypnotics

Hypnotic Drugs*	Half-life (hr)	Onset of Action (min) <sup>†</sup>	Pharmacologically Active Metabolites	Dose (mg)
Quazepam (Doral)	48-120	30	<i>N</i> -desalkyl (flurazepam)	7.5-15
Flurazepam (Dalmane)	48-120	15-45	<i>N</i> -desalkyl (flurazepam)	15-30
Triazolam (Halcion)	2-6	2-30	None	0.125-0.25
Estazolam (ProSom)	8-24	Intermediate	None	1-2
Temazepam (Restoril)	8-20	45-50	None	15-30
Flunitrazepam (Rohypnol)	10.7-20.3	Short	<i>N</i> -desmethyl (flunitrazepam)	0.5-1
Nitrazepam (Alodorm)	25-35	Intermediate	None	5-10

## Receptor Pharmacology of Sedating Antidepressant Drugs

Drug	Receptor Effects*						Other Effects
	NE Reuptake	5-HT Reuptake	5-HT <sub>2</sub> Receptor Antagonism	Alpha <sub>1</sub> Antagonism	M Antagonism (Anticholinergic)	H <sub>1</sub> Antagonism (Antihistaminic)	
Doxepin	+	0/+	+	+++	++	+++	
Amitriptyline	+	++	+	+++	+++	++	
Trimipramine	0	0	+	+++	++	+++	
Trazodone	0	+	++	++	0	0/+	5-HT <sub>2A</sub> , 5-HT <sub>1D</sub> , and alpha <sub>2</sub> antagonism
Nefazodone	0	++	++	++	0	+	
Mirtazapine	0/+	0	++	+	+	+++	Alpha <sub>1</sub> and 5-HT <sub>1</sub> antagonism

## Summary of Other Drugs Used to Treat Insomnia

Drug	t <sub>max</sub> (hr)	Metabolism	t <sub>1/2</sub> (hr)	Mechanism of Action
Melatonin	20-60 min	Conjugation; oxidation by CYP enzymes	40-60 min	Agonist at melatonin type 1 and type 2 receptors
Ramelteon	0.3 hrs	Extensive first-pass metabolism; hepatic oxidation primarily via CYP1A2; active metabolite M-II	1.2 (2-5 hours for M-II)	Agonist at melatonin MT <sub>1</sub> and MT <sub>2</sub> receptors
Diphenhydramine	2-2.5	Hepatic demethylation, oxidation	4-8	Antagonizes H <sub>1</sub> receptors
Valerian	Uncertain owing to multiple constituents	Uncertain owing to multiple constituents	Uncertain owing to multiple constituents	Uncertain; may increase GABA formation, interact with L-amino acid transporter receptor, or act as adenosine receptor agonist
Choral hydrate	Short	Converted to trichloroethanol, which undergoes conjugation	5-10 (for trichloroethanol)	Barbiturate-like effect at GABA <sub>A</sub> receptors
Quetiapine	1-2	CYP 3A4	6	Antagonizes H <sub>1</sub> , alpha <sub>1</sub> , M <sub>1</sub> , 5-HT <sub>2</sub> , D <sub>2</sub> receptors
Gamma-hydroxybutyrate	30-45 min	Metabolized to GABA, succinic semialdehyde, H <sub>2</sub> O and CO <sub>2</sub>	20-70 min	May act directly as neurotransmitter, increases brain dopamine levels

### The trial of infant response to diphenhydramine: the TIRED study--a randomized, controlled, patient-oriented trial *Merenstein et al 06*

- Double-blind, randomized, controlled clinical trial. 44 kids aged 6 to 15 months. Placebo or diphenhydramine given for a week
- Data safety monitoring board voted unanimously to stop the trial early because of lack of effectiveness of diphenhydramine over placebo. Only 1 of 22 children receiving diphenhydramine showed improvement compared with 3 of 22 receiving placebo.
- CONCLUSION: During 1 week of therapy and at follow-up 2 and 4 weeks later, diphenhydramine was no more effective than placebo in reducing nighttime awakening or improving overall parental happiness with sleep for infants.

## Peds Sleep Pharm

- There is a need for greater information on the pharmacological management of sleep disorders in children.
- Pharmacological guidelines need to be developed specifically for sleep disorders in children.
- These guidelines should FDA approved for the specific sleep disorder or for the pediatric age range. This will avoid physicians from being forced to prescribe medications as an "off label" indication.

## Peds Sleep Pharm

- Development of easy to swallow, chewable or liquid forms of these medications would be well received by parents everywhere. When these are not available, instructions for compounding these medications into a suspension by pharmacists are needed.
- Integration of behavioral and pharmacological treatments may yield better patient outcomes. This would require pediatricians to have a comprehensive understanding of clinical sleep disorders in children.
- Training programs should play lead role in enhancing pediatricians' knowledge of the pharmacological treatment of sleep disorders in children.

- **Non-pharmacological management of problematic sleeping in children with developmental disabilities.**

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