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Northern Institute for Organizational Capacity
Institut du Nord pour la Capacité Organisationnelle

nioc.ca

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Sleep 101 in Kids

Dr Colin M. Shapiro BSc, FRCPC, MBBS, PhD

http://www.sleepontario.com/

Mon, Sep 19, 2011

This presentation is brought to you in a collaboration between NIOC and Dr. Colin M. Shapiro

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Session Outline

A) Restorative Functions of Sleep
B) Impact of Obesity in Sleepiness in Children
C) Circadian Rhythms in Children
D) Academic Performance and Behaviour
E) Mood
F) Fetal Alcohol Syndrome
G) Prader Willi
H) Parasomnias in Children

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Sleep Ontario Clinics

For a Better and Healthier Sleep

Our Mission

To provide detailed conscientious care to people with any sleep & wakefulness problem irrespective of age.

Address: 227 Victoria Street,
Lower Level 2
Toronto, ON
M5B 1T8

Telephone: (416) 703-0505

Fax: (416) 703-0507

We conduct new patient consults and follow-up appointments:

Monday to Friday: 9:00 am to 5:00 pm

We conduct sleep studies seven days a week.

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The Wall of Evidence for The Restorative Theory of Sleep

Catabolism/anabolism*
The balance tips towards more build-up during sleep

Growth hormone
Mostly released at night and mostly in deep sleep

ATP† concentrations
Increase while oxygen consumption drops as during sleep

Oxygen
use decreases in deep sleep

Pregnancy
is associated with increased deep sleep

Illness
People with illnesses that lead to low energy output (e.g., paraplegics or those with hypothyroidism) have low levels of deep sleep

Exercise
People who exercise have more deep sleep, indicating that sleep is restorative

Immunology
Infected animals who are prevented from sleeping are more likely to die

Height
Teenagers get taller during the growth sleeping period

Core sleep
When sleep is lost, deep sleep is replaced first

Cell mitosis
Most cell division is during sleep

Recovery
There is more Deep Sleep after Deprivation

Memory
Growing evidence that certain types of memory need deep sleep

This figure emphasizes the points made on the previous page. There are many bricks in the wall of evidence that link sleep to a restorative process.

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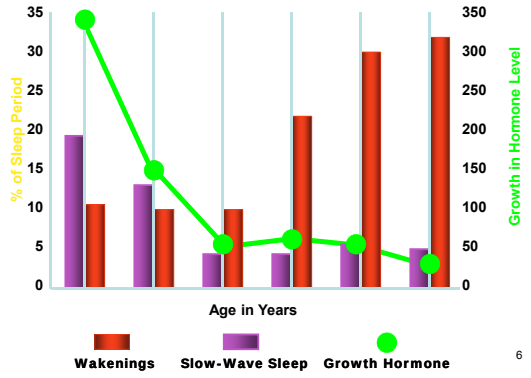
Changes in Sleep and Growth Hormone with Age



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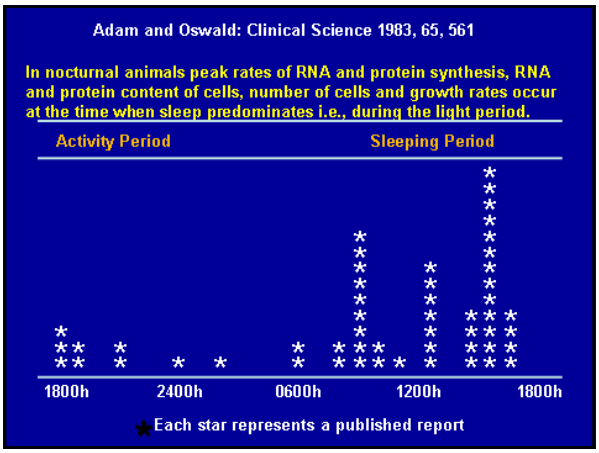
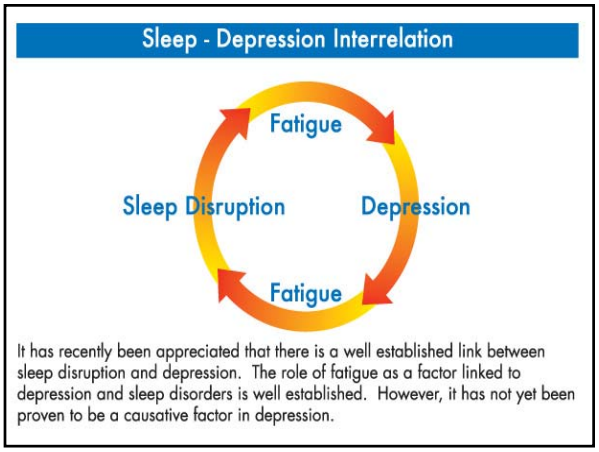
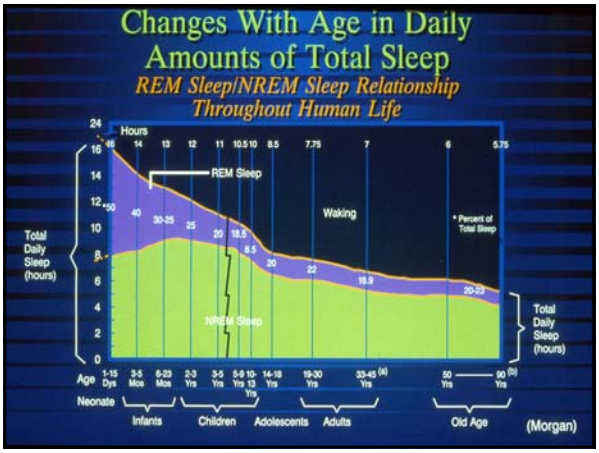
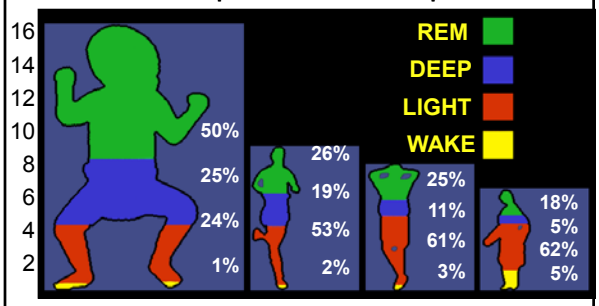

Adam and Oswald: Clinical Science 1983, 65, 561
In nocturnal animals peak rates of RNA and protein synthesis, RNA and protein content of cells, number of cells and growth rates occur at the time when sleep predominates i.e., during the light period.
Activity Period
Sleeping Period
1800h
2400h
0600h
1200h
1800h
Each star represents a published report

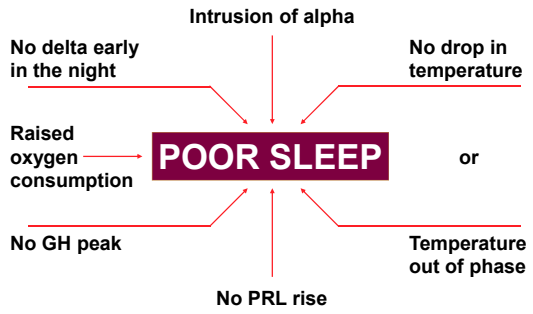

Sleep - Depression Interrelation
Fatigue
Sleep Disruption
Depression
Fatigue
It has recently been appreciated that there is a well established link between sleep disruption and depression. The role of fatigue as a factor linked to depression and sleep disorders is well established. However, it has not yet been proven to be a causative factor in depression.


Changes With Age in Daily Amounts of Total Sleep
REM Sleep/NREM Sleep Relationship Throughout Human Life
Hours
REM Sleep
Waking
NREM Sleep
Total Daily Sleep (hours)
Age
Neonate
Infants
Children
Adolescents
Adults
Old Age
(Morgan)

LIFE - Cycle and Sleep

Composition of Sleep





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What is a Sleep Disorder?

Anything that interferes with:

- Feeling Rested at Night
- Staying Awake & Alert during the Day

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Is Sleep a Problem?

Anything that interferes with:
- **Feeling Rested at Night**
- **Being Awake & Alert during the Day**

Problem → Interferes with School, Work or Family

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What are Common Sleep Disorders?

INSOMNIA
- **Difficulty Falling asleep**
- **Can't Stay asleep (keep waking up)**
- **Wake up too Early in the morning**
- **Sleep is not Refreshing**

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What are Common Sleep Disorders?

INSOMNIA
- **Difficulty Falling asleep**
- **Can't Stay asleep (keep waking up)**
- **Wake up too Early in the morning**
- **Sleep is not Refreshing**

❖ Can affect up to as many as 1 in 5 teens
❖ Signs: always Fatigued; Drinking too much Caffeine; Inattention; Irritable; Lack of *Get-up and Go*

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What are Common Sleep Disorders?

SLEEP APNEA

- Stop breathing for very short periods during the night

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What are Common Sleep Disorders?

SLEEP APNEA

- Stop breathing for very short periods during the night

- Signs: loud Snoring; Hyperactivity; Behavioural Problems (acting out, aggression, irritability, impulsivity); Poor Concentration & Memory; Unusual Sleeping Position

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Other Common Sleep Disorders?

NARCOLEPSY

- Can't stop sleeping

PARASOMNIA

- Walking, Talking during sleep

LIMB MOVEMENTS

- Kicking of legs during sleep

- Signs: Difficulty with Awakening in the Morning; very Sleepy during the day; Sheets all Disarranged in the morning

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Common Pediatric Conditions often Associated with an Underlying Sleep Disorder

Medical
- Gastroesophageal reflux
- Obesity
- Failure to thrive
- Musculoskeletal pains

Sleep-related
- Daytime sleepiness
- Snoring
- Restlessness during sleep
- Bedwetting

Behavioural or Psychological
- Hyperactivity and attention deficits
- Learning difficulties
- Reduced achievement at school
- Aggression
- Cognitive deficits
- Alcohol or drug use, cigarette smoking
- Depression
- Anxiety

Colin M. Shapiro and Johanna C. Goll *Canadian Medical Association Journal*, pg: 617-619, 2006

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CAN STRESS MESS UP YOUR SLEEP?

YES
- **Problems falling asleep (intrusive/circular thoughts)**
- **Wake up multiple times during the night**
- **Unrefreshing sleep**

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STRESS SOLUTIONS

TIPS
- **Relaxing activities before sleep**
- **Moderate, regular exercise**
- **Counting sheep**
- **Be Realistic!!**

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KIDS GETTING ENOUGH SLEEP?

Teenagers often sacrifice sleep time when it comes to making choices about time management.

But, teens need a lot more sleep than they often get.

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SLEEP DEBTCALCULATION

- Sleep Need: 9-10 hours
- Sleep Loss per Night: 2 hours
- Sleep Loss total for Weekdays: 10 hrs
- Sleep Loss per Month: 40 hours
- Cumulative Loss per Month= 4+ Nights of sleep

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WHAT DID WE FIND?

Sleep duration on school nights: **Way Too Short!!**

Half (54%) said that they had difficulty falling asleep at bedtime.

- 6 out of 10: **Excessively Sleepy** during school. Daily Problem for 1 in 7 teens
- **1 in 3** students admitted to **Falling Asleep in class** (28% reported taking naps at School)

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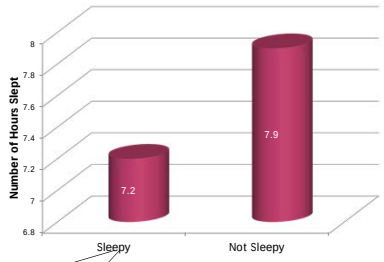
Less Sleep = More Sleepy



Girls

Grades 11 & 12

25

Academic Performance

Higher Mathematics grades

Improved Ability to Learn

Students whose Sleep Duration is appropriate for their age

Better Concentration & Memory

Less Behavioural &/or Conduct Problems

Higher GPA & IQ

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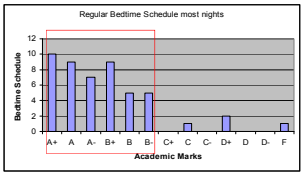
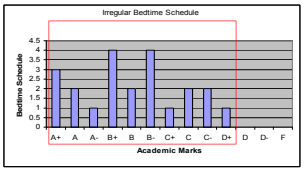
Academic Performance





Irregular Sleep Schedule was also linked with Poorer Academic Grades.

Don't Despair!!

Good Sleep Hygiene

→ Regular Sleep Schedule

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What is Sleep Hygiene???

DO's

- ☺ Regular bed & wake times
- ☺ Regular exercise
- ☺ Address stress
- ☺ Unwind before bedtime
- ☺ Keep a bedtime routine
- ☺ Take hot shower/bath before bed
- ☺ Talk to your family doctor about sleep problems
- ☺ Sleep in a comfortable bed
- ☺ Sleep in a quiet and dark bedroom

DON'Ts

- ☹ Exercise too close to bedtime
- ☹ Drink too much caffeine
- ☹ Smoke
- ☹ Have large meals too close to bedtime
- ☹ Drink alcohol later than 3 hours prior to bedtime
- ☹ Drink too much fluid too close to bedtime
- ☹ Nap where possible
- ☹ Take over-the-counter remedies for sleeplessness – get help from your doctor.
- ☹ Participate in stimulating activities before sleep (i.e. electronic devices, exciting books or TV shows, etc)

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Patient B.

- **15 year old girl (first seen when she was 13 year old)**
- **Long sleep duration reported by mother (up to 14 hours)**
- **Fell asleep in elementary school**
- **In Grade 5 she had difficulty falling asleep**
- **Going to bed at 5 am or 6 am**
- **Absence from school just at the time that she entered into adolescence**

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Patient B.

- Dim Light Melatonin Onset study
- She had absolutely no Melatonin secretion at all
- Melatonin was prescribed
- Secreted by the pineal gland
- Melatonin is produced to help our bodies regulate our sleep-wake cycles
- Darkness stimulates the release of melatonin and light suppresses its activity
- Melatonin cycles are disrupted when we are exposed to excessive light in the evening or too little light during the daytime

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Patient B.

- Sleep pattern changed
- Able to go to bed at about 9:00 pm instead of going to bed at 5-6:00 am

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- Features of Seasonal Affective Disorder (changes in mood, sleep, appetite with onset of winter)
- Bright light treatment

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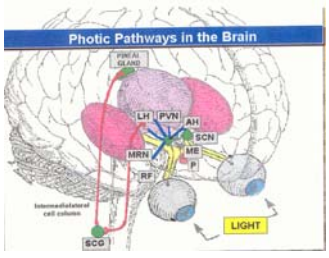
The Circadian Rhythm of Sleep

- The Suprachiasmatic Nucleus (SCN) is a pair of small pea-shaped structure composed of ten thousands of neurons.
-
- The optic nerves from both eyes join at the optic chiasm



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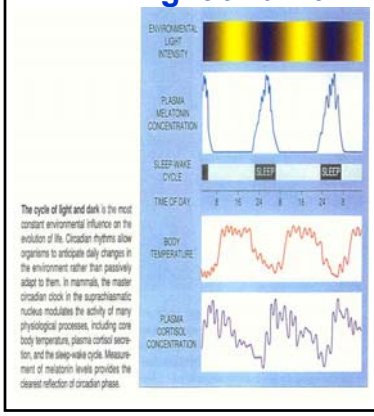
Light and Dark Cycle



- Synthesis and release of melatonin are stimulated by darkness and inhibited by light
- Decrease in body temperature during sleep

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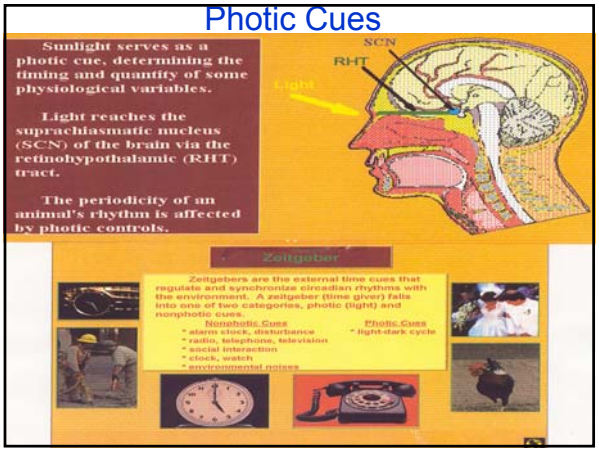
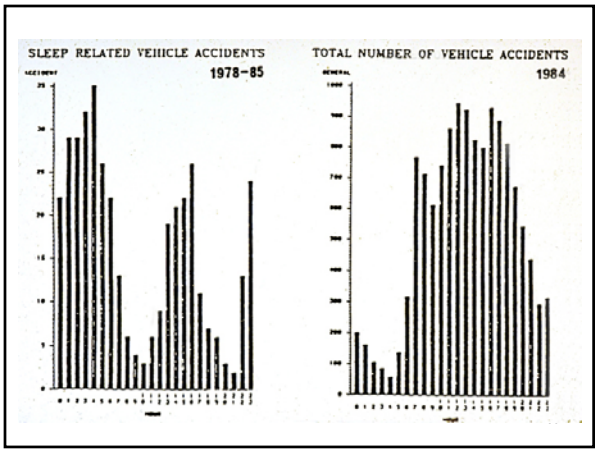
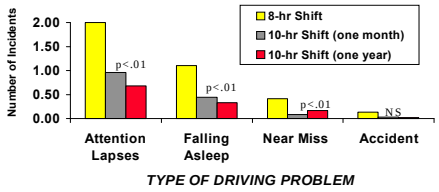
Photic Cues





Type of Driving Problem Reported During Night Shift Commuting



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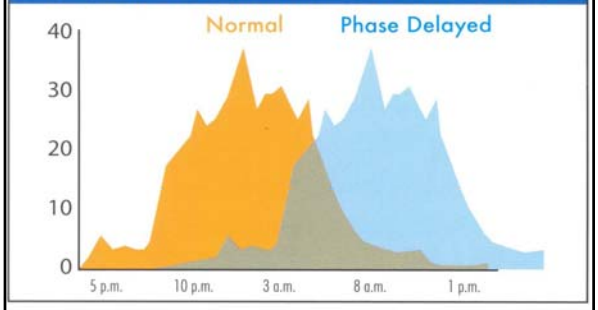
Melatonin Secretion to Measure Circadian Timing



The orange pattern (normal individual) shows Melatonin secretion with a abrupt rise at about 9:00 p.m. The blue pattern shows the Melatonin measurements in a teenager with phase delay syndrome where the abrupt rise in Melatonin levels occurs at 3:00 a.m.

- **PACKET "A" AND PACKET "B"**

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- REPORT CARD WITH E,E,E,E, (CLOSE TO FAIL)

40

CAVEATS

A) OLYMPIC SKIER

B) REPRODUCTIVE EFFECTS

C) MISUSE OF MELATONIN

Are there new treatments

41

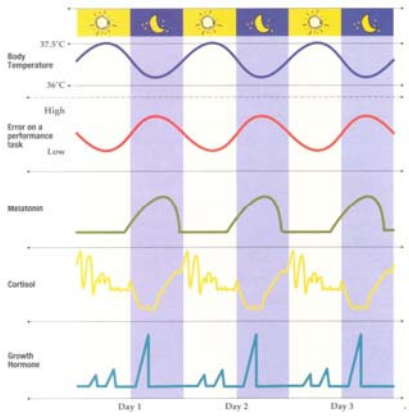
Earlier ('81) Clouston had similar thoughts

Clouston, T (1881)

Alternation, periodicity and relapse in mental diseases

Trans. Med-Chir.Soc.Edinburgh

42



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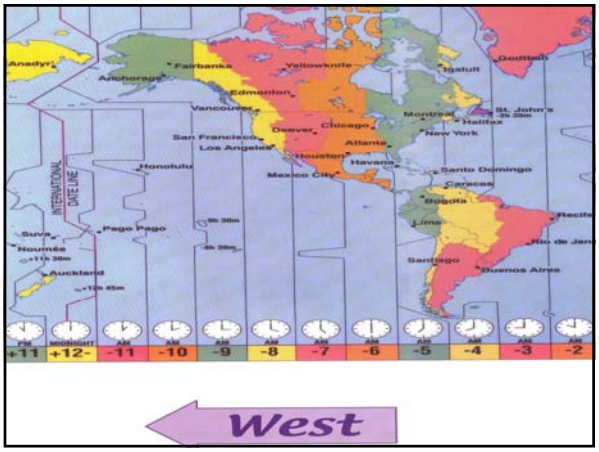
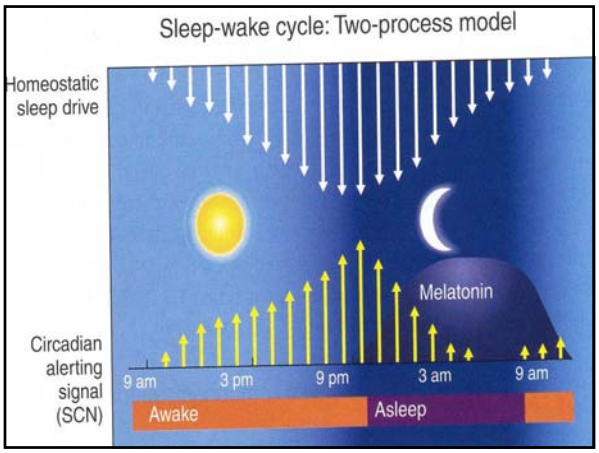
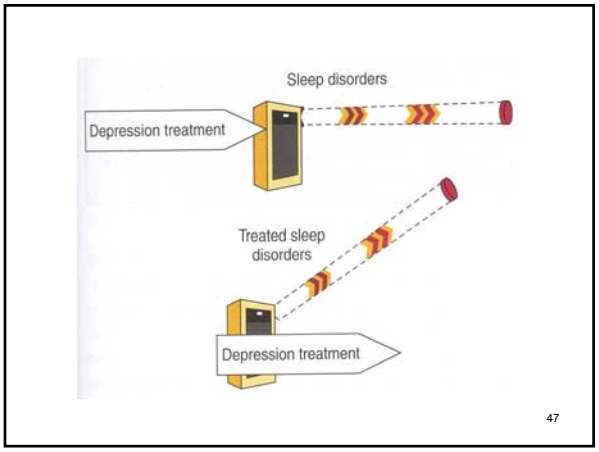
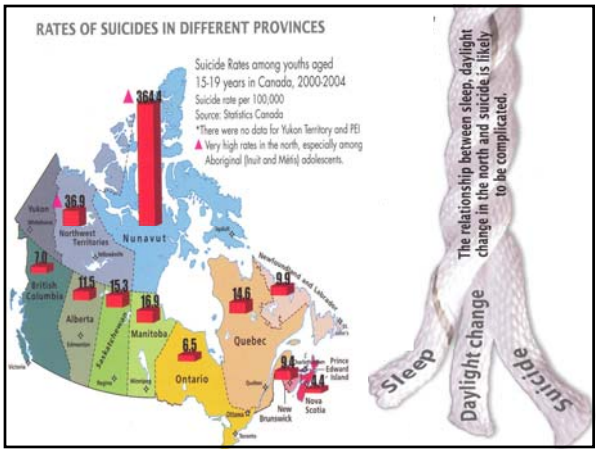


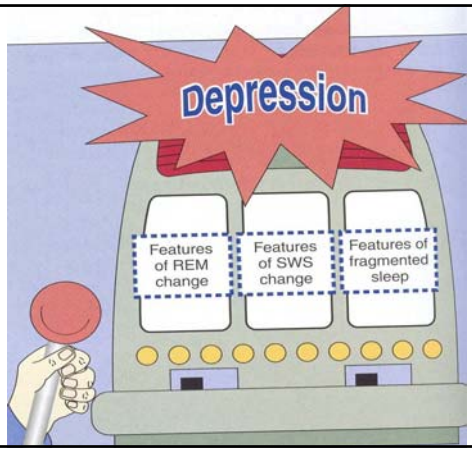
Jauhar, P and Weller, MPI (1982) Psychiatric morbidity and time zone changes : a study of patients from Heathrow Airport, Br.J. Psychiatry 140, 231-235

45


Sleep-wake cycle: Two-process model
Homeostatic sleep drive
Melatonin
Circadian alerting signal (SCN)
9 am
3 pm
9 pm
3 am
9 am
Awake
Asleep


Sleep disorders
Depression treatment
Treated sleep disorders
Depression treatment
47


RATES OF SUICIDES IN DIFFERENT PROVINCES
Suicide Rates among youths aged 15-19 years in Canada, 2000-2004
Suicide rate per 100,000
Source: Statistics Canada
*There were no data for Yukon Territory and PEI
▲ Very high rates in the north, especially among Aboriginal (Inuit and Métis) adolescents.
364.4
36.9
7.0
11.5
15.3
16.9
6.5
14.6
9.9
Yukon
Northwest Territories
Nunavut
British Columbia
Alberta
Saskatchewan
Manitoba
Ontario
Quebec
Newfoundland and Labrador
Prince Edward Island
Nova Scotia
New Brunswick
The relationship between sleep, daylight change in the north and suicide is likely to be complicated.
Sleep
Daylight change
Suicide



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Normal development

- Mid pregnancy- circadian cycles present.
- Circadian loss after birth
- 3-6 months – Sleep pattern appear
- Adolescents – Sleep time consistent
  Daytime sleep tendency rise
  Stay up late at night
  Wake up late in the morning

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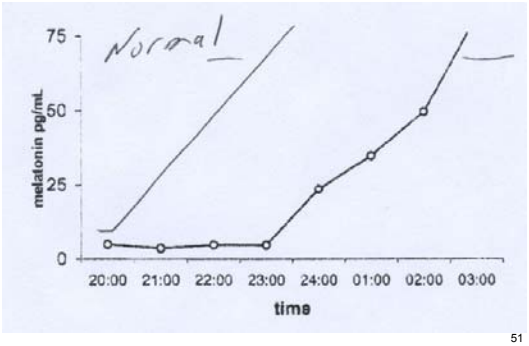
DLMO Graphs: Classic DSPS 1



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Sleep disorders in children with attention-deficit/hyperactivity disorder (ADHD)

Colin Shapiro[1, 3] and Rosalia Yoon[1, 2]
[1] Institute of Medical Sciences, University of Toronto
[2] Child, Youth and Family Service, Centre for Addiction and Mental Health
[3] Youthdale Child and Adolescent Sleep Clinic

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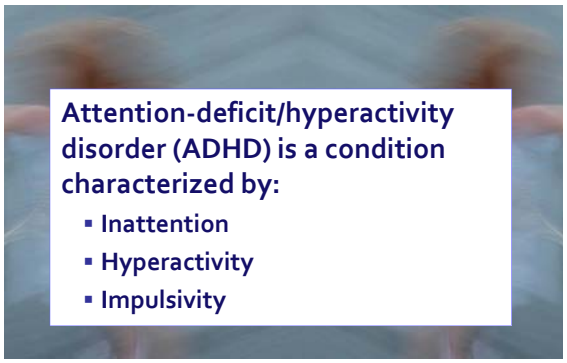
What is ADHD?



Attention-deficit/hyperactivity disorder (ADHD) is a condition characterized by:

- Inattention
- Hyperactivity
- Impulsivity

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Associated Symptoms

In some children and adolescents, ADHD can also be associated with

- Depression
- Anxiety
- Sleep disorders

About a third of children and adolescents with ADHD have been reported to have sleep problems!

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Prominent sleep problems in ADHD

- Delayed sleep onset
- Interrupted sleep
- Changes in sleep architecture
- Restless legs syndrome
- Sleep disordered breathing:
  - Snoring
  - Obstructive sleep apnea

Daytime symptoms of sleep problems in ADHD

- Difficulty getting up in the morning
- Difficulty getting to sleep
- Excessive daytime sleepiness
- Inattention
- Behavioural problems
- Irritability
- Hyperactivity
- Conduct problems

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Why is sleep important in ADHD?

Sleep disturbances can give rise to, or worsen ADHD-like symptoms

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Sleep disorders can give rise to, or worsen ADHD symptoms

- Studies have shown that poor sleep quality due to sleep disturbances can result in:
  - Errors in cognitive tasks
  - Inattention
  - Problems with behaviour
- Studies have shown that good sleep hygiene can improve attention and concentration tasks

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TAKE HOME MESSAGE

Sleep studies may be important tools for the diagnosis and treatment of ADHD, not only because sleep disturbances are common in ADHD, but also because improving sleep quality can significantly reduce symptoms associated with ADHD.

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British Medical Journal on: Sleeplessness

"The subject of sleeplessness is once more under public discussion. The hurry and excitement of modern life is quite correctly held to be responsible for much of the insomnia of which we hear; and most of the articles and letters are full of good advice to live more quietly and of platitudes concerning the harmfulness of rush and worry. The pity of it is that so many people are unable to follow this good advice and are obliged to lead a life of anxiety and high tension."

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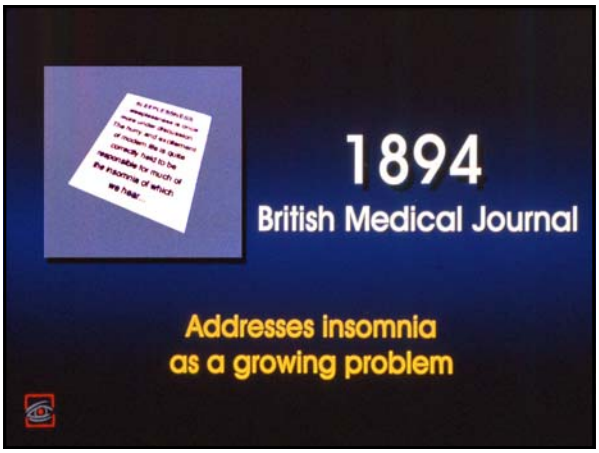
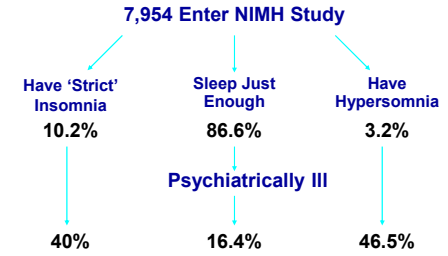
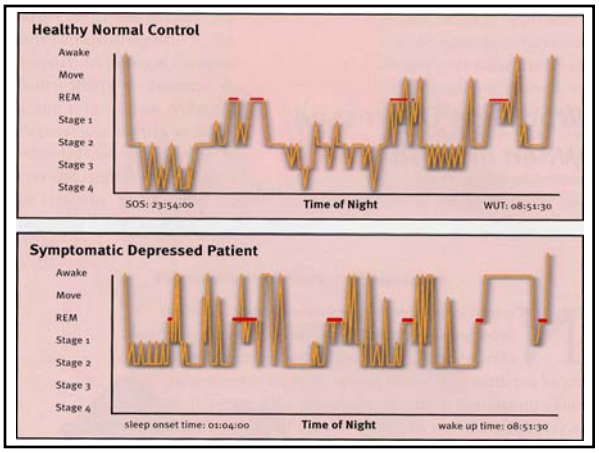


Epidemiologic Study of Sleep Disturbance and Psychiatric Disorders



Ford and Kamerow 1989

62



School-related Symptoms of Youth Depression

- Poor performance in school, truancy, tardiness
- Withdrawal from school activities/peer groups
- Lack of enthusiasm, energy or motivation
- Globalized anger and rage
- Overreaction to criticism, increased self-criticism
- Indecision, lack of concentration or forgetfulness
- Restlessness and agitation
- Problems with authority
- Suicidal thoughts or actions (e.g., cleaning out locker, giving away items)

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- Fear of failure
- social rejection
- bodily sickness
- bullying or abuse
- childhood memories
- thoughts of a better life
- separation with family
- worries about the future

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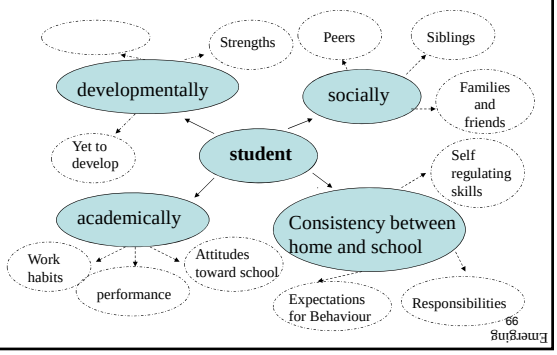
The Web of Behaviour



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Emerging

- This booklet was distributed to parents, school boards, family doctors, group practice and social workers .
- Response was positive and helped families in particular to accept the diagnosis and initiate treatment specifically.

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- Parents and health professionals were able to recognize the behavior in the children after reading this booklet.
- This educational tool also helped in the early recognition, detection and assessment of depression in children and teenagers at the sleep clinic.

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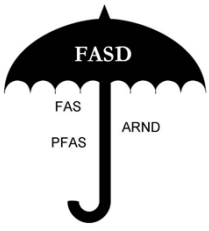
Background: What is FASD?

- FASD = Fetal Alcohol Spectrum Disorders
  - "is an umbrella term describing the range of effects that can occur in an individual whose mother drank alcohol during pregnancy" (Chudley *et al*. 2005)
  - Leading known preventable cause of birth defects (NOFAS, 2006)



Chudley A, Conry J, Cook J, Loock, Rosales, T, LeBlanc, N. *CMAJ* 2005; 172(5):S2-S21.

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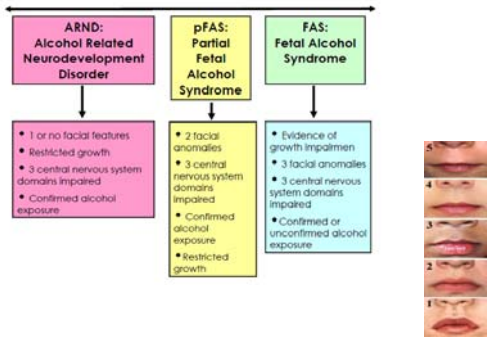
FAS SPECTRUM



Chudley A, Conry J, Cook J, Loock, Rosales, T, LeBlanc, N. *CMAJ* 2005; 172(5):S2-S21.

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What are the effects of FASD?

- Specific facial characteristics
- Growth deficits
- Hyperactivity & behavior problems
- Attention & memory problems
- Low IQ (~70)
- Poor coordination or motor skill delays
- Difficulty with judgment and reasoning
- Learning disabilities
- **Sleep and circadian rhythm disorders**

Almost every 8 in 10 children with FASD have a sleep complaint. *(Stade et al, 2008)*
75-80% prevalence of sleep disturbances in FASD children *(Jan et al, 2010)*

Stade B, Khuu D, Bennett, P, Sandor P, Stephens R, and Lanceta M. Sleep disturbances in children with fetal alcohol spectrum disorder (FASD). Paediatrics & Child Health 2008; 13

71

FASD AND SLEEP: What is Known?

- Despite the high % of sleep complaints, only a few studies have examined sleep in the FASD population:

Study	Main Findings	Limitations
1. "Sleep disturbances in children with fetal alcohol spectrum disorder (FASD)" *Stade et al, 2008*	- 82 of 100 caregivers of children between the ages of 5-8 reported sleep problems such as waking up more than twice a night, sleep terrors, and daytime fatigue	- Caregiver reports - No objective measures of sleep - Small range of ages (5-8 years)
2. "Sleep fragmentation and evidence for sleep debt in alcohol-exposed infants" *Troese et al, 2008*	- Increased sleep fragmentation and decreased REM sleep in infants whose mother's consumed alcohol during pregnancy	- Infant population - EEG of short naps - No overnight polysomnography
3. "Sleep Problems in Children With Prenatal Substance Exposure" *Stone et al, 2010*	- Of the 5 substances (including alcohol), prenatal nicotine exposure was the only unique predictor of sleep problems	- Maternal reports - No objective measures of sleep

What is Known? CNS Impairments

- Size reductions and irregularities in CNS structures
  (Chen *et al.*, 2003; Riley & McGee, 2005; O'Hare *et al.*, 2005)

- Neurotransmitter and neuroendocrine function disruptions
  - Growth deficiency (Thadani & Schanberg, 1979)

•Chen W.J., Maier S.E., Parnell S.E., West J.R., *Alcohol Research and Health 2003; 27:* 174-180.
•O'Hare E.D., Kan E., Yoshii J., Mattson S.N., Riley E.P., et al. *Neuroreport* 2005; 16: 1285-1290.
•Riley, E. P., McGee, C. L. *Experimental Biology & Medicine* 2005; 230: 357–365.
•Thadani, P. V., & Schanberg, S. N. *Neuropharmacology*, 1979; 18, 821-826.

RESULTS – SLEEP ARCHITECTURE

- Significant differences between the sleep architecture of FASD patients, compared to normative data

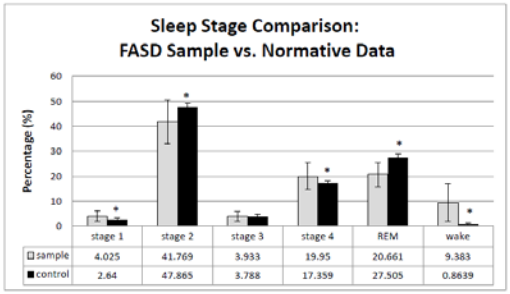

Figure 1: Distribution of sleep architecture percentages for FASD sample and normative data. (*) represent statistical significance ($p<0.001$), except for stage 4 ($p<0.05$)

RESULTS – DLMO

Twenty-four patients completed the DLMO test. The 24 melatonin phase-response curves were categorized into 4 main types:

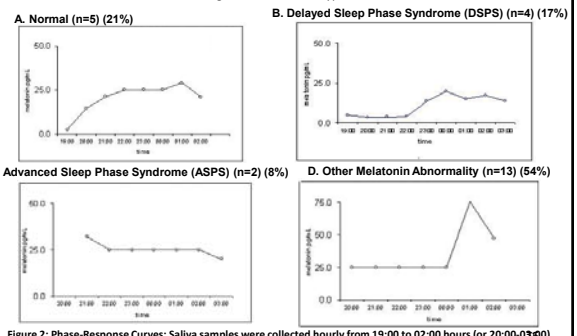

Figure 2: Phase-Response Curves: Saliva samples were collected hourly from 19:00 to 02:00 hours (or 20:00-03:00) and batch processed by Enzyme Linked Immunoassay Assay (ELISA)

RESULTS – Diagnoses of Sleep Disorders

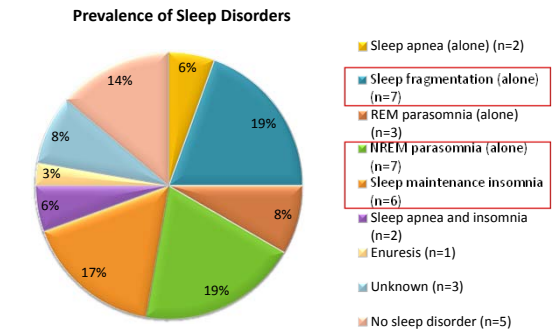

Figure 4: Prevalence of sleep disorders in total FASD sample (n=36).

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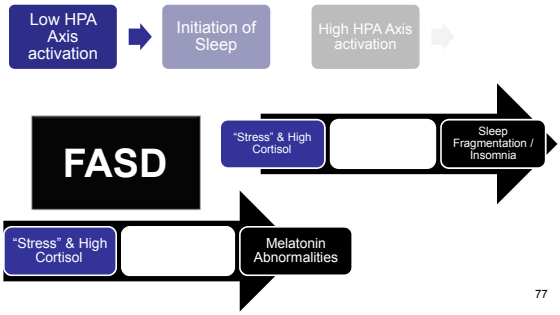
Possible Mechanisms

- **Altered HPA-axis function**
  - SCN located in hypothalamus



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Clinical Implications and Future Studies

- The increased prevalence of sleep disturbances in this population suggests the need for sleep assessments for children with FASD, and in the FASD diagnostic process
- Measure melatonin before medications are prescribed
- Follow-up sleep studies after treatments
- Improvements to other neurocognitive difficulties

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RESULTS –Circadian Rhythm Disorders

Prevalence of Circadian Rhythm Disorders

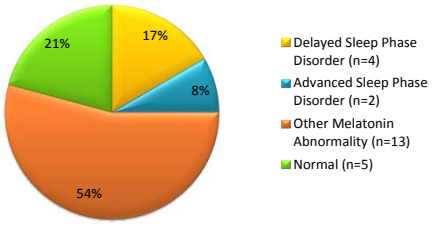
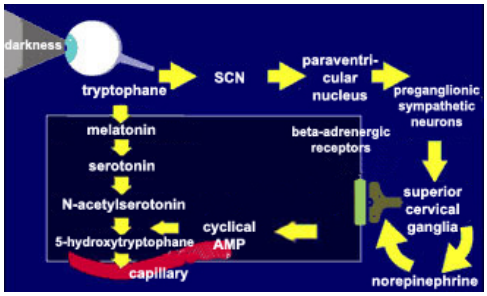


Figure 3: Prevalence of circadian rhythm disorders and other melatonin abnormalities based on melatonin profiles (n=24)

79



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Prader-Willi Syndrome

- genetic disease
- hypotonia,
- developmental delay, failure to thrive,
- ↑appetite, obesity,
- sleep apnea, excessive daytime sleepiness

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- Tryptophan was prescribed
- Less tired in class
- More able to do activities at the end of the day
- Does not fall asleep on the TTC

Tryptophan

- one of the 20 amino acids
- dietary sources: oats, bananas, milk, yoghurt, cottage cheese, eggs, fish, chckpeas, red meat, sunflower seeds
- possibly increases brain levels of serotonin and/or melatonin

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83

SLEEPWALKING

Simple Automatic Activities

Do Not Respond

Do Not Remember

They Are Not Dreaming!

84

Why is Sleep Important ?

- Growth
- Energy, Restoration (Deep Sleep,Cell Division, Pregnancy, Marathon)
- Mood
- Sleepiness
- Fatigue
- Performance
- Circadian Rhythm Of Body, Organs,Cells
- Immune Function
- Disorders

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Why is Sleep Important For Teenagers ?

- **Growth**
- **Peformance (School)**
- **Behaviour**
- **Mood**
- **Energy – Sports**
- **Appetite – Weight Control**
- **Memory Learning**

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Case 1: 'Andrew'

Sleep Study: Tuesday

Study Start: 9:30pm
Sleep Latency: 14 min
REM Latency: 74 min
Sleep Stages: Normal for age
Arousal Index: 18/hour
AHI: <1/hour
PLMS: 2/hour

MSLT:

Time	9am	11am	1pm	3pm	
SOL	7 min	2 min	4 min	11 min	mean 6 min

No REM sleep

What would you do?

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Case 1: 'Andrew' (cont'd)

Andrew has an increasing dose of tryptohopan over a 12-week period. The final dose is 3 grams one hour before bedtime

Parents note a clear improvement.

Teacher is so moved with results: writes to sleep clinic.

Repeat Sleep Study: Friday

Study Start: 9:30pm
SOL: 8 min
REM Latency: 82 min

Sleep Stages: Normal for age
Arousal Index: 2/hour
AHI: <1/hour
PLMS: 2/hour

MSLT:

Time	9am	11am	1pm	3pm	
SOL	-	-	18 min	-	mean 19.5 min

No REM sleep

No Sleep Fragmentation = Sleepiness gone!

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Case 2: 10-20 years

Cathy, 17 yrs old. Seen in another sleep clinic for 'insomnia'. Following consultation, they note:

- She goes to bed 1-2am weeknights and has a hard time getting up for school.
- She goes to sleep on weekends at 2-4am and sleeps in late.
- Tired during daytime.

Sleep Study (at that clinic):

Study Start: 11pm
SOL: 194 min
REM Latency: 62 min

Sleep Stages: Disrupted
AHI: 0/hr
PLMS: 6/hour
Arousal Index: 26/hour

MSLT: Not done

Patient was prescribed zopicline: did not help! Sleep diary not kept. Told of website for sleep hygiene. No further help offered in that clinic.

What would you do?

89

Case 2: 'Cathy' (Cont'd)

We did a sleep consultation.

Phase Delay seemed most likely (not considered in other clinic's report).

Protocol of 2 nights:

1st Night

PSG: "Early" sleep bedtime before midnight

Night 1 Results:
Low sleep efficiency; prolonged SOL
High arousal rate (21/hr)

Day

MSLT

MSLT Results:
SOL: 13 minutes av.
(SOL for 4 sessions: 5min, 8min, 17min, no sleep)
No REM

2nd Night

DLMO: 7pm-3am
PSG: 3:30-10:30am

DLMO Results: Clearly delayed melatonin onset

Night 2 Results:
Normal sleep efficiency
High arousal rate (18/hr)
REM onset early

What would you do?

90

Case 2: 'Cathy' (Cont'd)

Single-Blind melatonin/placebo administration:

- Clear positive response to melatonin
- Remained on melatonin for 1 year

Repeat Sleep Study: Wednesday (on melatonin)

Study Start: 11pm
SOL: 19 min
REM Latency: 96 min

Sleep Stages: Normal for age
AHI: 0/hr
PLMS: 4/hour
Arousal Index: 18/hour

MSLT:

Time	9am	11am	1pm	3pm	
SOL	-	-	19 min	-	mean 19.75 min

No REM sleep

No Complaints!

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Bedtime Schedule vs. BMI

Sleep Schedule	Avg. BMI (kg/m2)
Regular	20.5
Mostly Regular	20.6
Not usually Regular	22.7
Never Regular	23.8

Note that an Irregular Bedtime Schedule is associated with a greater **Body Mass Index** (BMI).

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Excessive Daytime Sleepiness in Children and Adolescents across the Weight Spectrum

Lilach Kamer, MD,
MSc candidate, IMS UoT.
Dr. Colin Shapiro, MD, PhD.
supervisor.

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Background

- Obesity in Children and Adolescents
- Excessive Daytime Sleepiness (EDS)
- Obesity ⟺ EDS.

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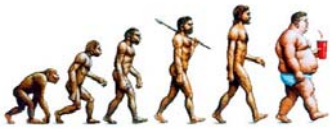
Overweight & Obesity



2004 Canadian Community Health Survey:

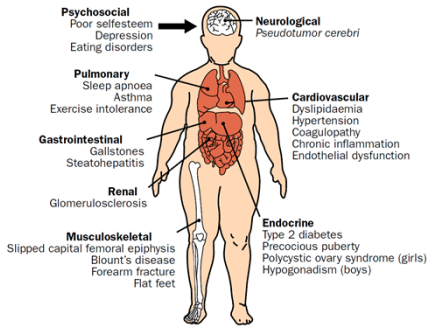
Adults
- 59% overweight (BMI>25 kg/m2)
- 1 in 4 (23%) is obese (BMI>30 kg/m2).

Children (2-17y/o)
- 1 in 4 (26%) overweight or obese.
- Obesity rate increased over 15 years: 2% to 10% boys; 2% to 9% girls.

(Lau et al, 2007).

95

COMPLICATIONS OF CHILDHOOD OBESITY



Ebbeling et al. 2002

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Excessive Daytime Sleepiness (EDS)

- **A tendency to fall asleep inappropriately.** (Objective) — Multiple Sleep Latency Test (MSLT)
- **Mental and physical abilities.** (Subjective) — Questionnaires (Carskdon 2005; Shen 2005)

- **Prevalence** in children and adolescents: **17-68%.**

(Gibson et al. 2006; Kothare 2008) 97

Causes

- Poor sleep habits.
  - Sleep time restriction.
- Sleep pathology.
- Medical condition.
- Medications.

(Fallone 2002; Pagel 2009). 98

Consequences of EDS

- **Social embarrassment**
- **Impaired daytime function**
- **Lower scholarly achievements**
- **Mood** (e.g. anxiety and depression).
- **Life threatening** (e.g. motor vehicle accidents).

(Smedje 2001, Chervin 2001, Fallone 2002; Pagel 2009). 99

Obesity ⟺ EDS

Independent of Sleep Apnea

In adults: Sloan and Shapiro 1995; Vgontzas et al. 1998; Resta et al. 2001; Resta et al. 2003; Bixler et al. 2005.

In children and adolescents:

little is currently known.

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Obesity & EDS in Paediatric Literature

	Marcus, 1996	Gozal, 2001	Gozal, 2009	Tsaoussoglou, 2010
Number of subjects	22 OB subjects	92 OW/OB subjects- 54 OSA, 14 snoring, 24 control	100 OB subjects- 50 subject with SDB, 50 control	150 subjects- 76 NW controls, 42 OW/OB controls, 32 OW/OB subjects with OSA.
Age (years)	2-20	6-9	6-9	5-17
Measure of EDS	MSLT	MSLT, Subjective measures used but not reported.	MSLT	Subjective measure (Parental reports – PSQ).
Population source	Primary care clinic	Sleep clinic	Sleep clinic	Sleep clinic
Conclusion	Correlation between EDS and obesity	Correlation between EDS and obesity, EDS and OSA, each independently.	In any severity of OSA obese children exhibit more daytime sleepiness	Obesity and not the severity of sleep disorder is associated with sleepiness
Limitations	No control group, small sample size coupled with wide age range.	Focus on SDB, much smaller sample size for the snoring and the control group.	Focus on SDB.	No objective sleepiness measurement.

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Hypothesis:

Children and adolescents who are overweight or obese **will exhibit more EDS** compared to normal-weight aged matched individuals, independent of measures of sleep pathology.

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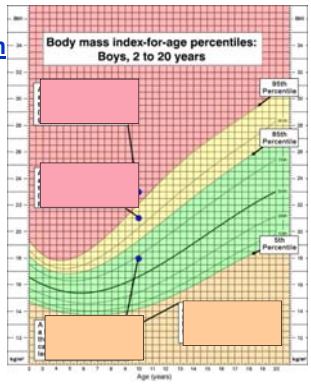
Weight Group Definition

The BMI percentile (BMI%) for age and gender was calculated for each participant.

Overweight (OW): 85% <BMI%≤ 95%.

Obese (OB): BMI%> 95%



CDC growth charts, USA 2000. 103

Weight Groups

- Overweight and obese groups were merged into one group named the **Overweight range (OWr)** group.

Normal weight (NW)- BMI% ≤ 85%.
Overweight range (OWr)- BMI%>85%.

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Multiple Sleep Latency Test (MSLT)

The most widely used validated objective measure of EDS.

- After an overnight sleep study
- 4-5 nap opportunities, 20 minutes each.
- Mean Sleep Latency (MSL) is calculated.

(MSL range 0-20)

Sleep latency- *time from lights off until the first epoch of that can be scored as any stage of sleep.*

Adults- *MSL under 11 minutes indicates EDS*

(Arand et al. 2005, Shen 2005, Carskadon 1982)

105

Pediatric MSLT

No normative criteria.

- At the Youthdale Child and Adolescents Sleep Center:

'Abnormal' MSLT result:
Age<13 MSL_{MSLT} < 19 minutes.
Age≥13 MSL_{MSLT} < 16 minutes.

(based on the longer MSL_{MSLT} in pre- or early pubertal children, clinical impression and personal communications with specialists in the field of pediatric sleep analysis)

(Carskadon 1982; Kotagal 1996) 106

1350 Files reviewed.

↓

466 MSLT performed, age 6-18y

↓

-15 Missing data

-195 Excluded for medical conditions and specific sleep disorders

↓ → -68 Excluded for use of sleep related medication- data from these files was later analysed as a separate group.

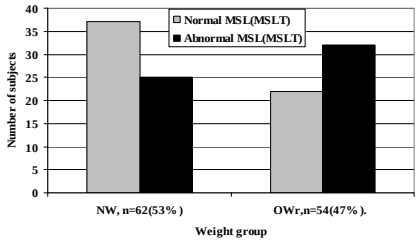
188 final population

107

Main analysis, Males, n=116.

Significant.

Frequency of normal vs. abnormal MSL_{MSLT} in each weight group.



Mean MSL_{MSLT}

NW
17.3 ±3.7

OWr
15.4 ±4.7

Z=2.08, **p=.04**

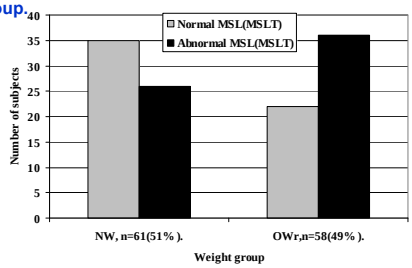
Normal MSL_{MSLT} (C: ≥19 A: ≥16), Abnormal MSL_{MSLT}(C:<19min A:<16min).
NW=Normal Weight group, OWr= Overweight and obese group.
Frequency of abnormal MSL_{MSLT}, 40% NW vs. 59% OWr, $\chi 2$ (2)=4.14, p=.042. 108

[Females, n=72, $\chi 2$ (2)=.13, p=0.71]

Main analysis, Age group C(<13y), n=119.

Significant.

Frequency of normal vs. abnormal MSL_{MSLT} in each weight group.



Mean MSL_{MSLT}

NW
18.4 ±2.2

OWr
16.5 ±3.7

Z=2.71, **p=.007**

Normal MSL_{MSLT} (C: ≥19 A: ≥16), Abnormal MSL_{MSLT}(C:<19min A:<16min).
NW=Normal Weight group, OWr= Overweight and obese group.
Frequency of abnormal MSL_{MSLT}, 43% NW vs. 62% OWr, $\chi 2$ (2)=4.5, p=.034.

[Age group A, n=69, $\chi 2$ (2)=0.9, p=0.77]

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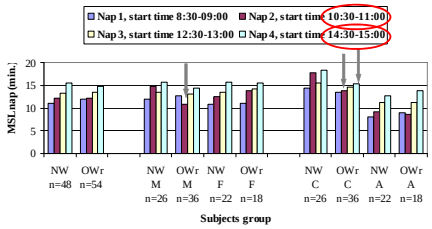
MSLnap by subjects weight, gender and age group



NW=Normal Weight, OWr=OW range, M=males, F=females, C=group C, A=group A.

Males

2nd nap (z=2.30, p=.02)

C age group

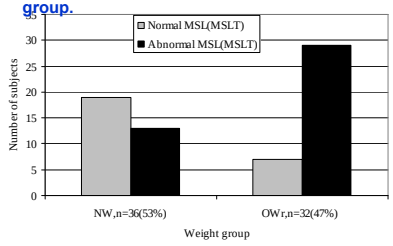
2nd and 4th nap (Z=2.74, p=.006 and Z=2.11, p=.035 respectively).

110

Secondary analysis- medicated subjects, n=68.

Significant

Frequency of normal vs. abnormal MSL_{MSLT} in each weight group.



Mean MSL_{MSLT}

NW
16.4 ± 4.9

OWr
12.9 ± 5.8

Z=3.06, **p=.002**

Normal MSLMSLT (C: ≥19 A: ≥16), Abnormal MSLMSLT(C:<19min A:<16min).
NW=Normal Weight group, OWr= Overweight and obese group.

Frequency of abnormal MSL_{MSLT} , 41% NW vs. 80% OWr, $\chi 2$ (2)=4.5, p=.031.

111

Strengths

- The largest sample of paediatric MSLT
  (almost double, in general and in relation to weight).
- Wide age range.

Contributes to the strength of the results

- Not only SDB/OSA patients. → The first time in pediatrics that this question is examined beyond SDB/OSA
- In concordance with previously published research.
- First- diurnal patterns of EDS in relation to weight. → A possible contribution to academic issues in OWr
- First- objective EDS & weight in children treated with psychiatric mediations.

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EDS & Weight: Adult literature

Resta et al, 2003.

- NW vs OB w/o diagnosed sleep disorder. PSG. EDS by ?.
- OB w/o OSA had finding similar to OB w OSA: low REM and SE.=> OB per se not OSA may be the reason.
- 35% of OB w/o OSA reported EDS per ?, vs 2.7 in NW controls.

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Sleep & obesity - Suggested pathogenesis

- Alterations in glucose metabolism.
- Up regulation of appetite.
- Decreased energy expenditure.

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Alterations in glucose metabolism

- Partial sleep deprivation=> acute **reduction in insulin release**, disturbances in the secretory profiles of the **counter-regulatory hormones** such as the growth hormone and cortisol (Knutson et al. 2007).
- Obesity as a **pro-inflammatory condition**. Inflammatory state affects the metabolic processing of glucose (Knutson et al. 2007; Alam et al. 2007).

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Up regulation of appetite

- Sleep restriction in healthy young volunteers => disregulation of neuroendocrine control of appetite, negative alteration in glucose tolerance. (Van et al. 2007).
- **Changes in the levels of appetite inhibiting or stimulating** hormones, such as Leptin and Ghrelin, with sleep deprivation (Knutson et al. 2007).
- **Hypocretin** (also known as Orexin), a neurotransmitter found in the hypothalamus- has moderate appetite stimulating properties. **Changes in its expression** in narcolepsy, Klein-Levin syndrome and Prader-Willi at times when symptoms of disturbed sleep exists (Ganjavi and Shapiro 2007).

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Decreased energy expenditure

- A Reduction in physical activity and energy is often reported by subjects with sleep problems and/or excessive daytime sleepiness. **Direct impact of sleep impairment.** (Scarpace et al. 1997; Tang-Christensen et al. 2004).

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