

Future Directions in Sleep and Developmental Psychopathology



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National Jewish Health
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Conflict of Interest Disclosures

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- National Institutes of Health
- Robert Wood Johnson Foundation

Consultant

- Johnson and Johnson

Royalties

- Co-author, *Pediatric Sleep Problems: A Clinician's Guide to Behavioral Interventions*

What is sleep and why is it important?

Which came first, the chicken or the egg?

Questions for today's talk

Are developmental changes during sleep important?

Sleep and developmental psychopathology, nature or nurture?

Sleep Primer





What is Sleep?

- Sleep is a **Go to sleep and wake up** of **Tune the world out** from and **relative insensitivity to the environment**, usually characterized by typical behavioral **cc** **Lie down with eyes closed**

What is Sleep?

- Sleep is a reversible behavioral state of perceptual disengagement from and relative insensitivity to the environment, usually characterized by typical behavioral concomitants

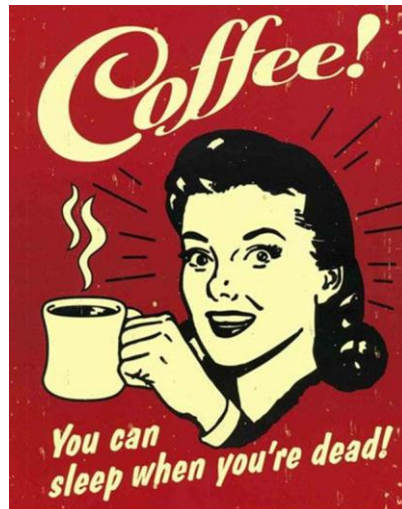
Sleep is not an optional luxury, but is essential for health, daytime functioning, and well-being

You have to breathe

You have to eat

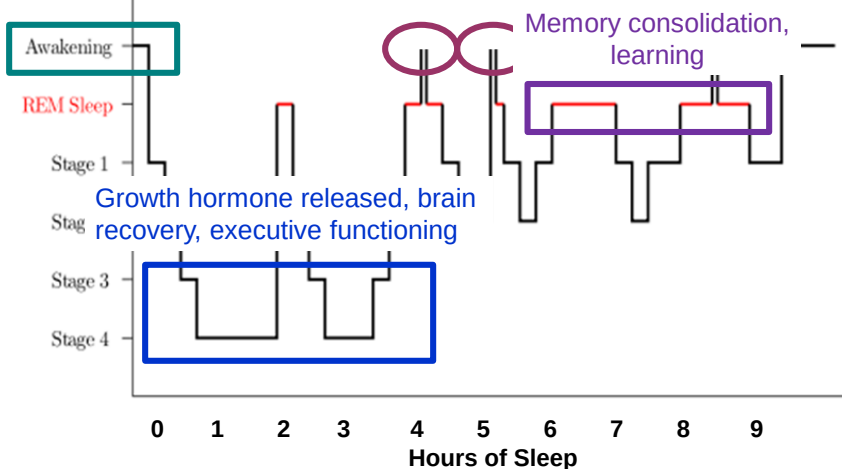
You have to sleep!

Sleep is NOT for slackers!

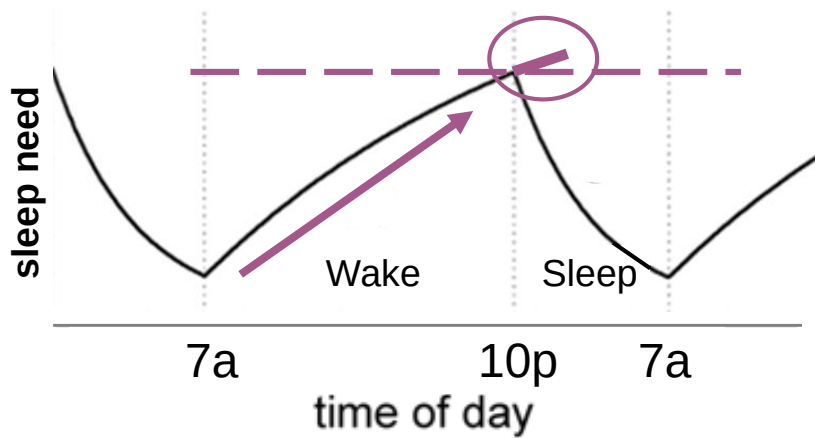


Stages of Sleep

Hypnogram

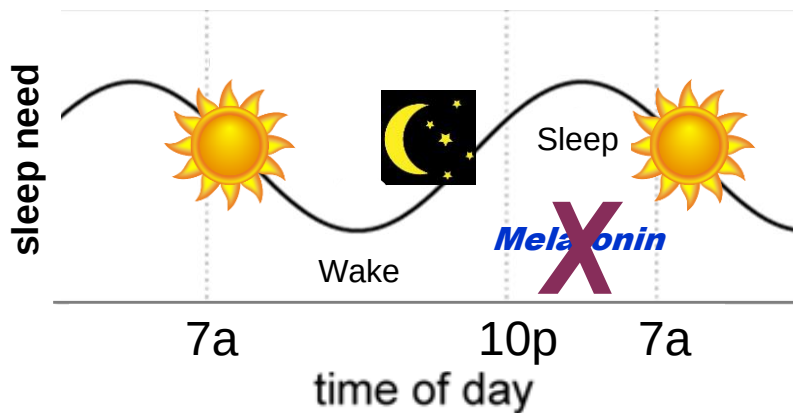


Process S – Sleep Homeostasis

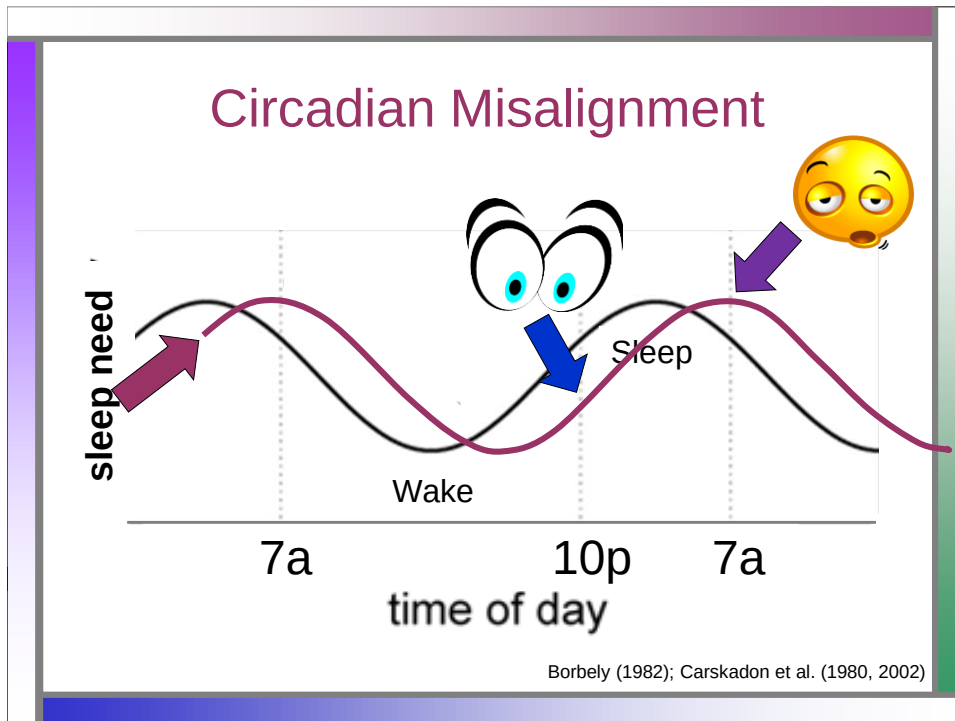


Borbely (1982); Van Dongen et al. (2003)

Process C - Circadian Rhythm



Borbely (1982); Carskadon et al. (1980, 2002)



Recommended Sleep Duration (2016)

JCSM
Journal of Clinical
Sleep Medicine

CONSENSUS STATEMENT

**Recommended Amount of Sleep for Pediatric Populations:
A Consensus Statement of the American Academy of Sleep Medicine**

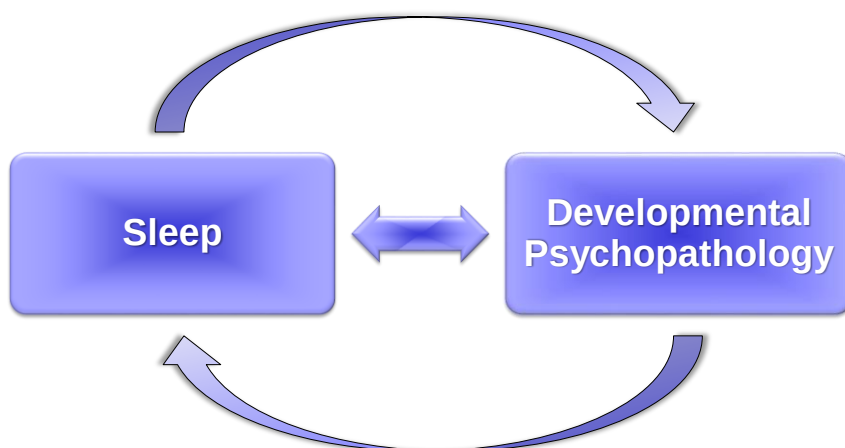
Shalini Paruthi, MD^{1,*}; Lee J. Brooks, MD^{2,3}; Carolyn D'Ambrosio, MD⁴; Wendy A. Hall, PhD, RN⁵; Suresh Kotagal, MD⁶; Robin M. Lloyd, MD⁷; Beth A. Malow, MD, MS⁷; Kiran Maski, MD⁸; Cynthia Nichols, PhD⁹; Stuart F. Quan, MD¹⁰; Carol L. Rosen, MD¹¹; Matthew M. Trøester, DO¹²; Merrill S. Wise, MD¹³

	Age	Sleep Per 24 Hours (*including naps)
Infants	4 to 12 months	12 to 16 hours*
Toddlers	1 to 2 years	11 to 14 hours*
Preschoolers	3 to 5 years	10 to 13 hours*
Children	6 to 12 years	9 to 12 hours
Adolescents	13 to 18 years	8 to 10 hours

Faces Associated with Insufficient Sleep



The Obvious Question



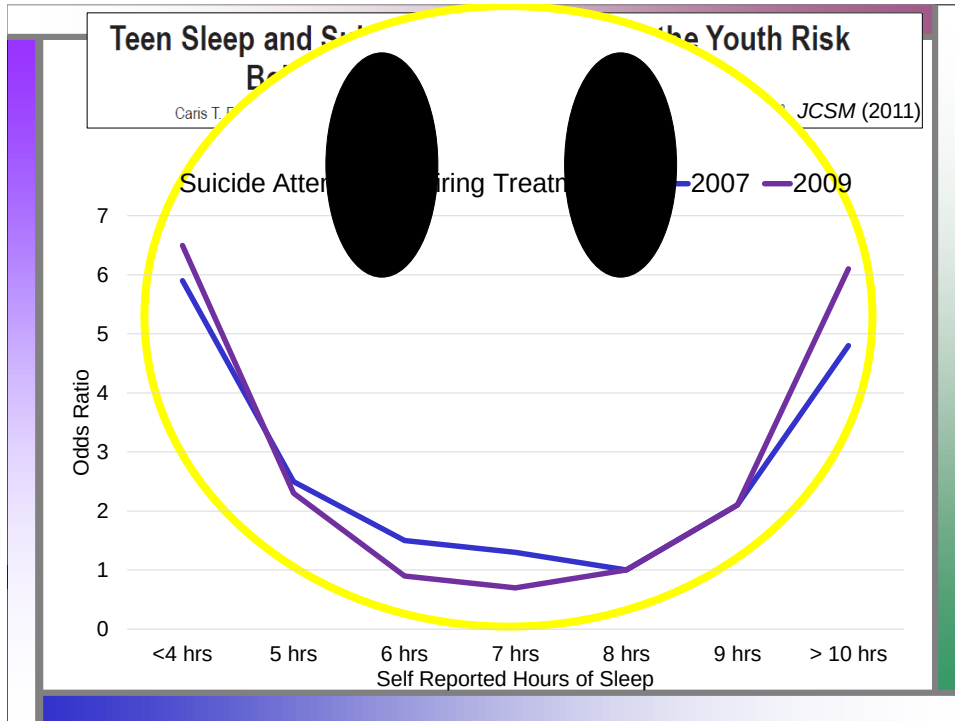
Future Direction #1

Answering the Obvious Question



Answering the Obvious Question

- Cohort studies

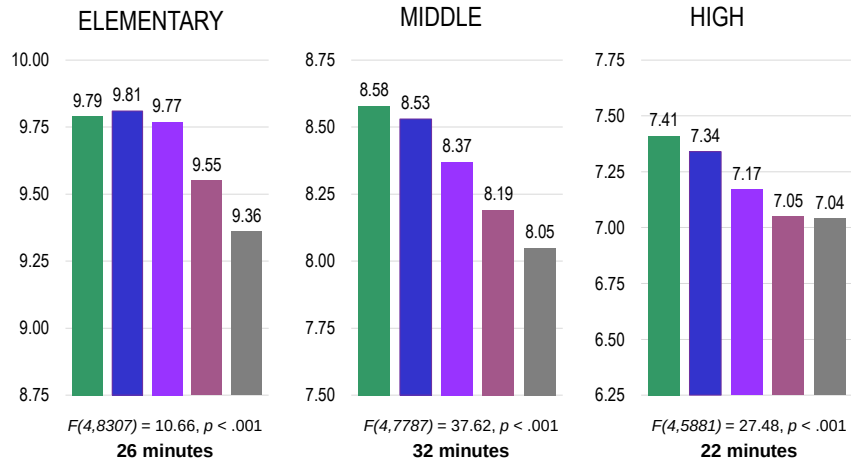


School Cohort

GRADE	FEMALE	WHITE	BLACK	HISPANIC	FREE REDUCED LUNCH
3 RD (n=3082)	47.9	54.9	8.8	18.7	30.5
4 TH (n=3090)	46.2	54.4	9.6	18.2	32.1
5 TH (n=3147)	47.5	56.1	9.8	19.3	30.8
6 TH (n=2936)	50.0	54.7	10.7	18.6	30.3
7 TH (n=2768)	49.1	54.8	10.9	18.6	30.5
8 TH (n=2738)	52.7	55.8	9.2	19.1	29.8
9 TH (n=2472)	50.9	53.6	11.2	19.8	31.5
10 TH (n=2004)	52.5	52.9	11.3	18.6	24.5
11 TH (n=1982)	53.9	53.3	11.5	18.2	26.0
TOTAL (n=24,219)	49.8	54.6	10.2	18.8	29.9

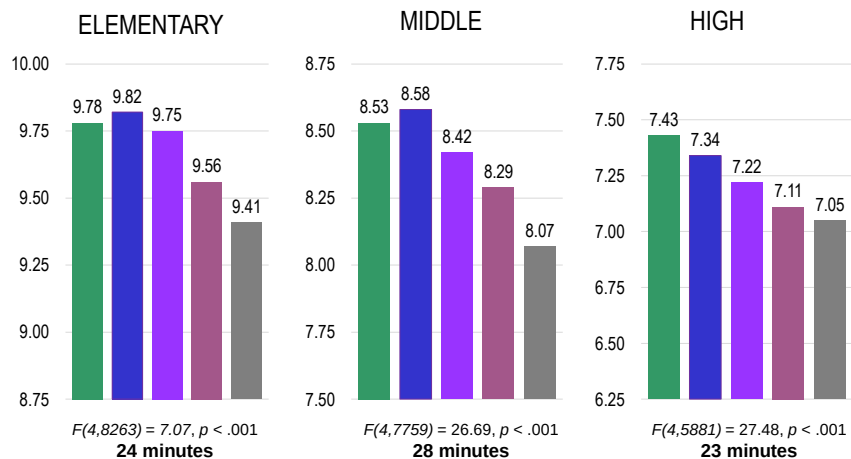
Weekday Sleep Opportunity (Hrs) and Sad in Past 7 Days

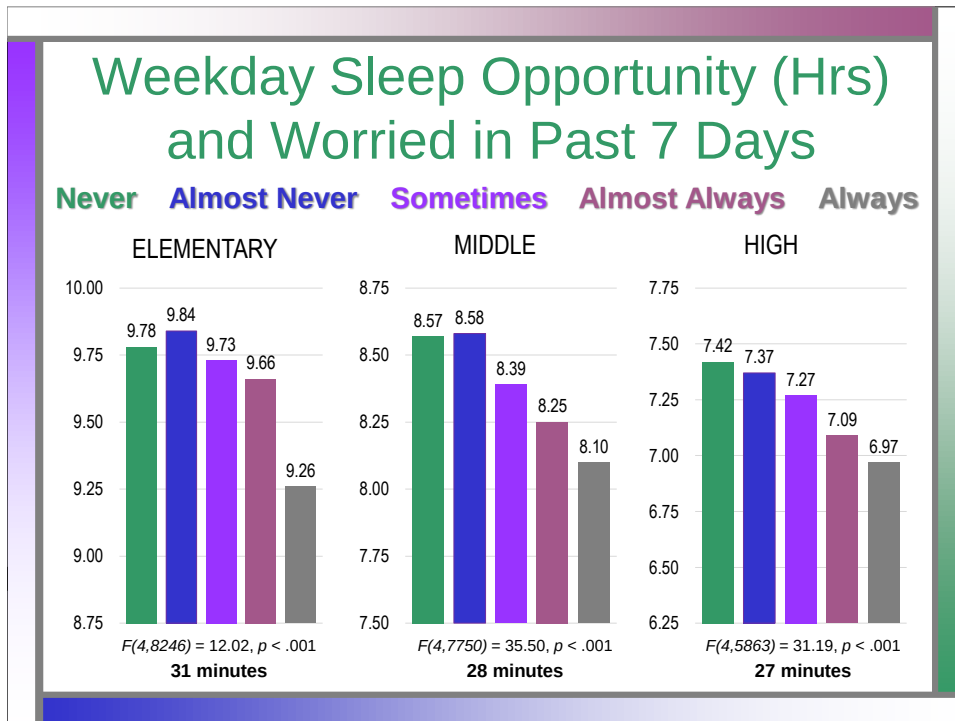
Never Almost Never Sometimes Almost Always Always



Weekday Sleep Opportunity (Hrs) and Nervous in Past 7 Days

Never Almost Never Sometimes Almost Always Always





Answering the Obvious Question

- Cohort studies
- Prospective studies

The Prospective Association between Sleep Deprivation and Depression among Adolescents

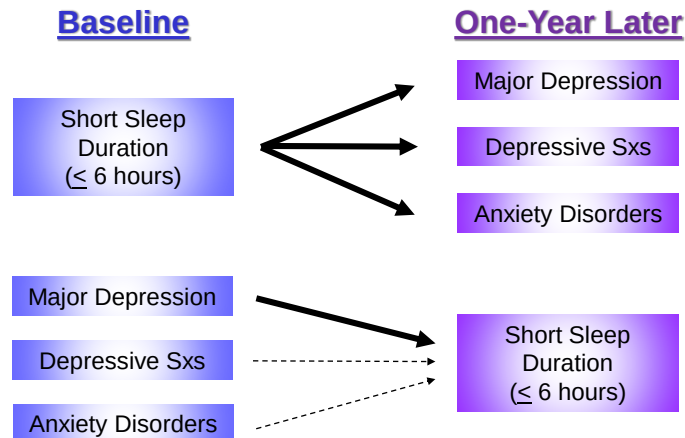
Robert E. Roberts, PhD¹; Hao T. Duong, MD, MPH, DrPh²

Sleep (2014)

Is there an association between short sleep duration and adolescent anxiety disorders?

Robert E. Roberts ^{a,*}, Hao T. Duong ^b

Sleep Medicine (2017)



Answering the Obvious Question

- Cohort studies
- Prospective studies
- Sleep manipulation protocols

Impact of Sleep Extension and Restriction on Children's Emotional Lability and Impulsivity

AUTHORS: Reut Gruber, PhD,^{a,b} Jamie Cassoff, BSc,^{a,b}
Sonia Frenette, PhD,^c Sabrina Wiebe, MSc,^{a,b} and Julie
Carrier, PhD^{c,d}

Pediatrics (2012)

Baseline Sleep (5 nights) via actigraphy

Sleep Extension
(+1 h sleep, 5 nights)
(n=17)

27 min increase

Sleep Restriction
(-1 h sleep, 5 nights)
(n=16)

54 min decrease

TABLE 3 Teacher-Reported CGI-T Scores of Children After Baseline and Sleep Manipulation

CGI-T Scores	Sleep-Extension Group		Sleep-Restriction Group	
	Baseline	After Sleep Manipulation	Baseline	After Sleep Manipulation
Emotional lability subscale	50.33 (8.29)	47.33 (4.65)	47.93 (6.23)	51.5 (7.85)
Restless-impulsive behavior subscale	49.94 (9.32)	47.05 (5.94)	51.94 (9.64)	55.06 (10.52)
Total score	49.89 (8.15)	46.67 (5.36)	50.44 (8.83)	54.19 (9.93)

Data are given as mean (SD).

Impact of sleep restriction versus idealized sleep on emotional experience, reactivity and regulation in healthy adolescents

RADHIKA REDDY^{1,2}, CARA A. PALMER¹, CHRISTINE JACKSON¹,
SAMANTHA G. FARRIS^{1,3} and CANDICE A. ALFANO¹

J Sleep Res (2017)

Baseline Sleep (6 nights) via actigraphy

Ideal Sleep
(9.5 h TIB, 1 night)

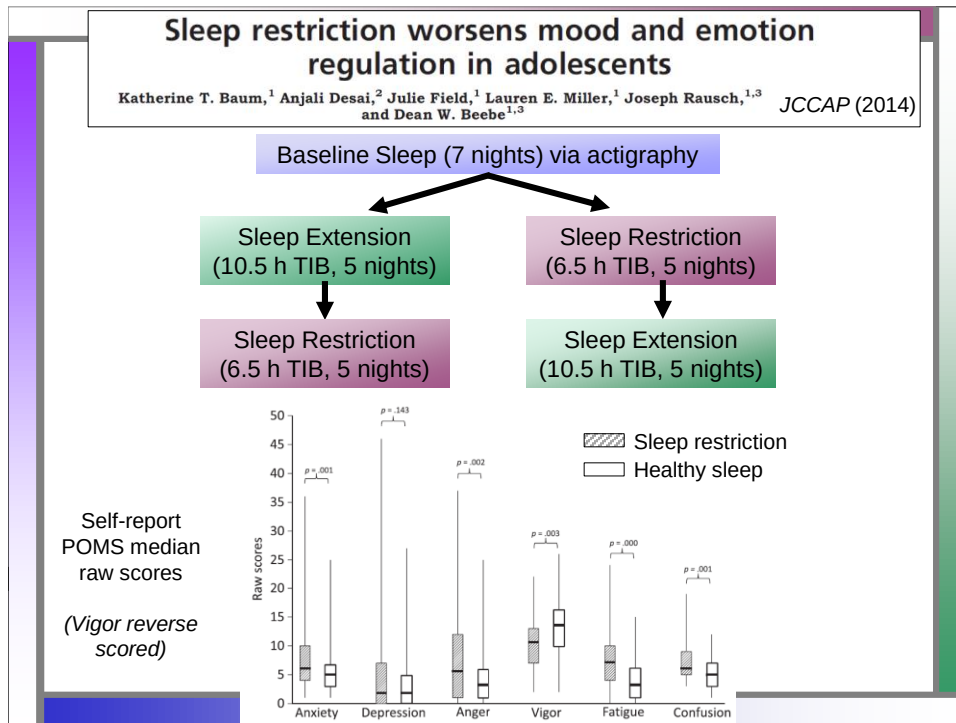
Sleep Restriction
(4 h TIB, 1 night)

Lab based emotional reactivity
Cognitive reappraisal

Table 4 Descriptive means for emotional reactivity variables for the full sample and two sleep conditions and comparisons between sleep groups

Variable (mean/SD)	Full sample (N = 42)	Restricted sleep group (n = 21)	Idealized sleep group (n = 21)	F _(1,40)	η^2_p (90% CI)	P
Valence						
Negative images	3.06 (0.76)	2.84 (0.69)	3.27 (0.77)	3.72	0.09 (<0.01, 0.24)	0.06
Neutral images	5.10 (0.38)	5.05 (0.32)	5.16 (0.44)	0.91	0.02 (<0.01, 0.14)	0.35
Positive images	7.59 (0.84)	7.51 (0.68)	7.67 (0.98)	0.35	0.01 (<0.01, 0.10)	0.56
Intensity/arousal						
Negative images	4.58 (1.69)	4.27 (1.81)	4.89 (1.54)	1.41	0.03 (<0.01, 0.16)	0.24
Neutral images	1.99 (1.22)	1.76 (0.85)	2.22 (1.49)	1.50	0.04 (<0.01, 0.16)	0.23
Positive images	4.83 (2.06)	4.51 (1.87)	5.15 (2.24)	1.00	0.02 (<0.01, 0.14)	0.32

Higher valence rating = more positive valence; Higher intensity/arousal rating = greater intensity/arousal. Means for negative images presented here were based on negative view images only.
SD, standard deviation; CI, confidence interval.



Future Direction #1

Answering the Obvious Question

- Population based studies highlight important associations
- Prospective studies help us understand directionality
- Sleep manipulation protocols identify underlying mechanisms

Future Direction #2

What Goes on During Sleep?



Mapping of Cortical Activity in the First Two Decades of Life: A High-Density Sleep Electroencephalogram Study

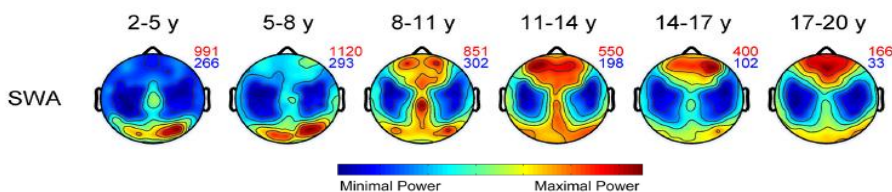
Salomé Kurth,¹ Maya Ringli,¹ Anja Geiger,^{1,2} Monique LeBourgeois,^{3,4} Oskar G. Jenni,^{1,2} and Reto Huber^{1,2}

J Neurosci (2010)

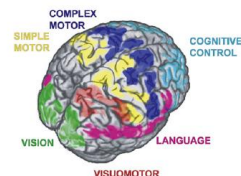
Mapping the electrophysiological marker of sleep depth reveals skill maturation in children and adolescents ☆

Salomé Kurth,¹ Maya Ringli,¹ Monique K. LeBourgeois,^{2,3} Anja Geiger,¹ Andreas Buchmann,⁴
Oskar G. Jenni,^{1,2} Reto Huber^{1,2,*}

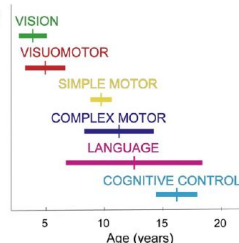
Neuroimage (2012)



B



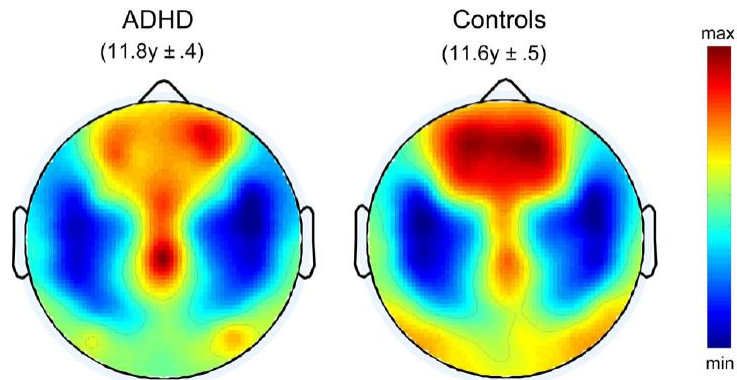
C



Topography of sleep slow wave activity in children with attention-deficit/hyperactivity disorder

Maya Ringli^a, Soraya Souissi^a, Salomé Kurth^a, Daniel Brandeis^{b,c,d}, Oskar G. Jenni^{a,d,f}
and Reto Huber^{a,d,e,f,*}

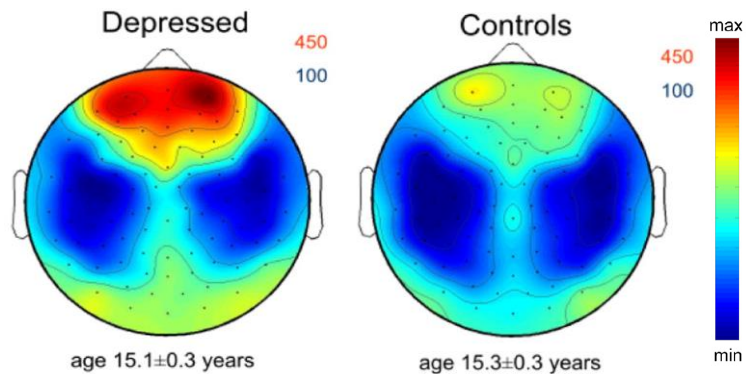
Cortex (2013)



Increased frontal sleep slow wave activity in adolescents with major depression

Noemi Tesler^{a,b}, Miriam Gerstenberg^c, Maurizia Franscini^c, Oskar G. Jenni^{a,d},
Susanne Walitza^{b,c,d}, Reto Huber^{a,b,c,d,*}

NeuroImage: Clinical (2016)

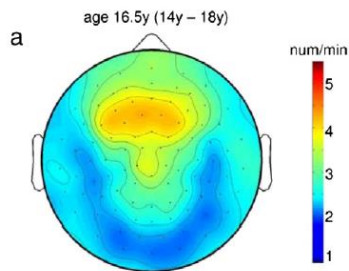


Reduced sleep spindle density in early onset schizophrenia: A preliminary finding

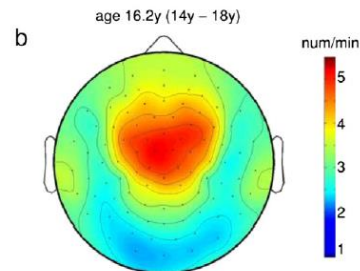
Noemi Tesler^{a,b}, Miriam Gerstenberg^c, Maurizia Franscini^c, Oskar G. Jenni^{a,d},
Susanne Walitza^{b,c,d}, Reto Huber^{a,b,c,d,*}

Schizophrenia Research (2015)

Early Onset Schizophrenia (EOS) patients



Healthy controls



Future Direction #2

What Goes on During Sleep?

- How can learning about biological changes during sleep across development assist with the diagnosis and treatment of psychopathology?

Future Direction #3

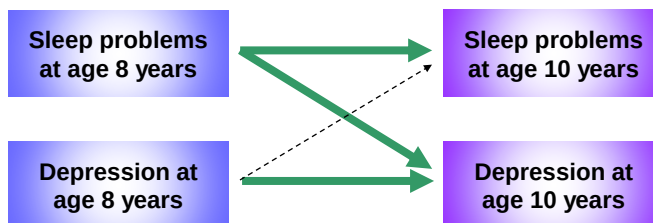
Nature vs. Nurture



The Direction of Longitudinal Associations Between Sleep Problems and Depression Symptoms: A Study of Twins Aged 8 and 10 Years

Alice M. Gregory, PhD¹; Fröhling V. Rijdsdijk, PhD²; Jennifer Y. F. Lau, PhD³; Ronald E. Dahl, MD⁴; Thalia C. Eley, PhD²

Sleep (2009)

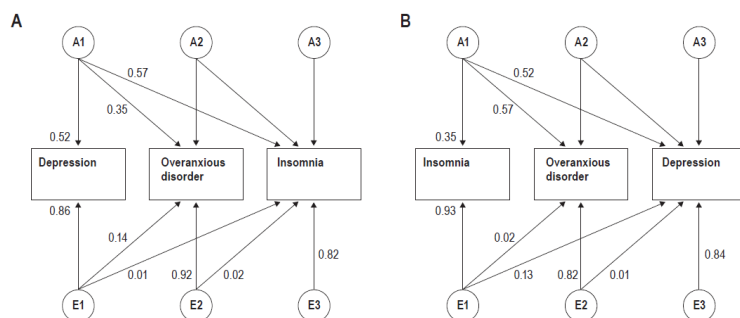


- Genetics most important in explaining stability of sleep problems
- Non-shared environment strongest influence on stability of depression
- Early treatment of sleep problems might protect against depression

Heritability of Insomnia Symptoms in Youth and Their Relationship to Depression and Anxiety

Philip R. Gehrman, PhD^{1,3}, Lisa J. Meltzer, PhD², Melisa Moore, PhD³, Allan I. Pack, MBChB, PhD^{3,4}, Michael L. Perlis, PhD¹, Lindon J. Eaves, PhD⁵, Judy L. Silberg, PhD⁵
Sleep (2011)

- Heritability of insomnia moderate (genetic factors accounted for 37% of variance)
 - Heritability of overanxious disorder: 30% M / 46% F
 - Heritability of depression: 11% M / 19% F



ADHD and Sleep Quality: Longitudinal Analyses From Childhood to Early Adulthood in a Twin Cohort

Alice M. Gregory, Jessica C. Agnew-Blais, Timothy Matthews, Terrie E. Moffitt & Louise Arseneault

JCCAP (2017)

- Childhood ADHD predicted poor sleep quality in young adulthood
 - After adjusting for adult ADHD diagnosis, childhood ADHD no longer associated with sleep quality at age 18 years
- ***If childhood ADHD remits, no increased risk of sleep problems as young adult***
- Young adult ADHD associated with poor sleep quality, due to genetic (55%) and non-shared environmental (45%) influences

Adolescents need 8.5 to 9.25 hours of sleep per night

7 out of 10 adolescents in the US get 7 hours or less per night



Carskadon et al. (1980, 2002), McKnight-Eily et al. (2011), NSF (2006, 2014), Owens et al. (2014), CDC (2018)

Extrinsic Sleep Disruptors





Goal SH-3: Increase the proportion of students in grades 9 through 12 who get sufficient sleep (8 or more hours of sleep on an average school night)

Baseline: 30.9% **Target:** 33.1%

- Sleep health education
- Changing school start times

Cherry Creek School District: Changing School Start Times

	2016 – 2017	2017 - 2018
High	7:10 a.m. to 2:30-2:51 p.m.	8:20 a.m. to 3:30 p.m.

Cherry Creek School District: Changing School Start Times

	2016 – 2017	2017 - 2018
High	7:10 a.m. to 2:30-2:51 p.m.	8:20 a.m. to 3:30 p.m.
Middle	7:50-8:10 a.m. to 2:50-3:10 p.m.	8:50 a.m. to 3:45 p.m.

Cherry Creek School District: Changing School Start Times

	2016 – 2017	2017 - 2018
High	7:10 a.m. to 2:30-2:51 p.m.	8:20 a.m. to 3:30 p.m.
Middle	7:50-8:10 a.m. to 2:50-3:10 p.m.	8:50 a.m. to 3:45 p.m.
Elementary	9:00 a.m. to 3:30 p.m.	8:00 a.m. to 2:45 p.m.

- Multi-method pre-post evaluation implemented
 - Surveys
 - Focus groups and open-ended surveys (including mental health team)
 - District level data (i.e., attendance, tardies, nursing records)
 - Community data (e.g., CDOT, law enforcement)

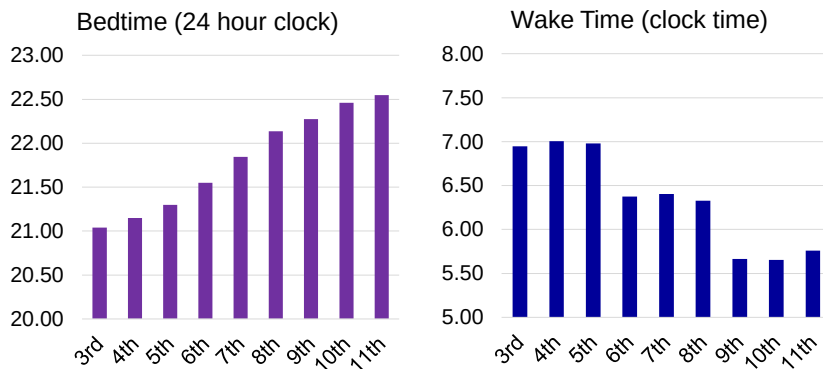
Cherry Creek School District: Changing School Start Times

Sample	2017	2018
All Students	25,446 (71%)	30,946 (76%)
Cohort Students	5327 (21%)	TBD
Parents	14,776 (32%)	11,144 (24%)
Staff	1,864 (53%)	2109 (58%)

- Reported bedtime and wake time for weekday and weekend
- PROMIS items for sleep, mood, health
- Additional questions about physical and academic health

Sleep Timing/Wake Time is Driven by School Start Times (pre)

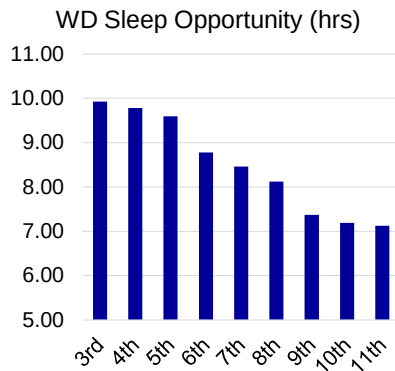
- Bedtimes increase steadily with increasing grade
 - ES → MS: 40 m, MS → HS: 34 m
- Wake times consistent across school level
 - ES: 6:58, MS: 6:33, HS: 5:41



Sleep Timing/Duration is Driven by School Start Times (pre)

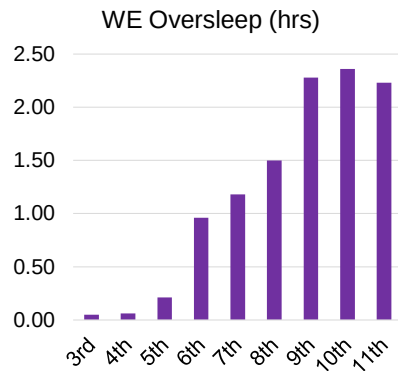
- Deficient sleep in high school students

■ 26.8% >8 hours of sleep



- Significant oversleep in older students

■ 2+ hours sleep deprivation

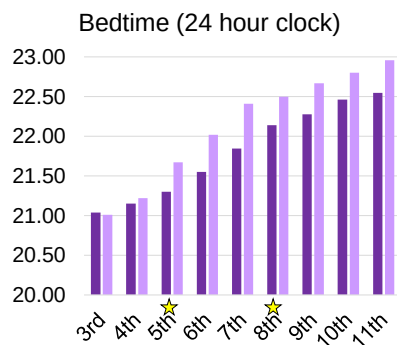


Sleep Timing/Wake Time is Driven by School Start Times (pre/post)

- Bedtimes increase steadily with increasing grade

■ ES → MS: 40 m, MS → HS: 34 m

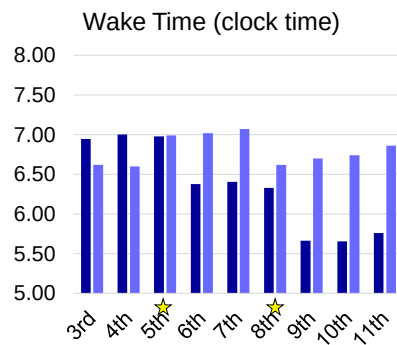
■ ES → MS: 66 m, MS → HS: 32 m



- Wake times consistent across school level

■ ES: 6:58, MS: 6:33, HS: 5:41

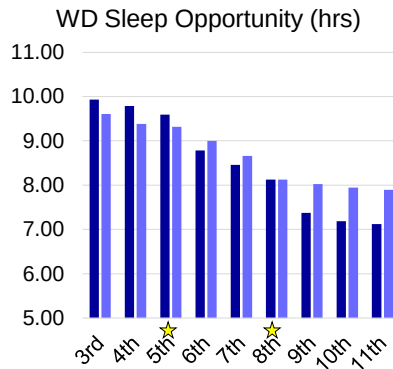
■ ES: 6:44, MS: 6:55, HS: 6:45



Sleep Timing/Duration is Driven by School Start Times (pre/post)

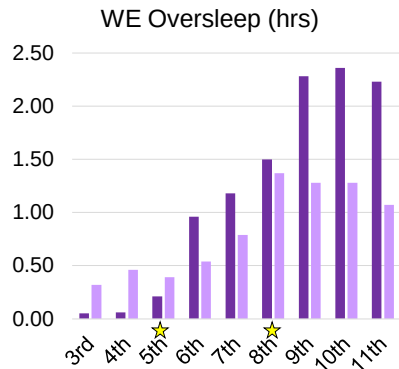
- Changes in weekday sleep opportunity

■ ES: -22 m, MS: +12 m, HS: +44 m



- Changes in amount of weekend oversleep

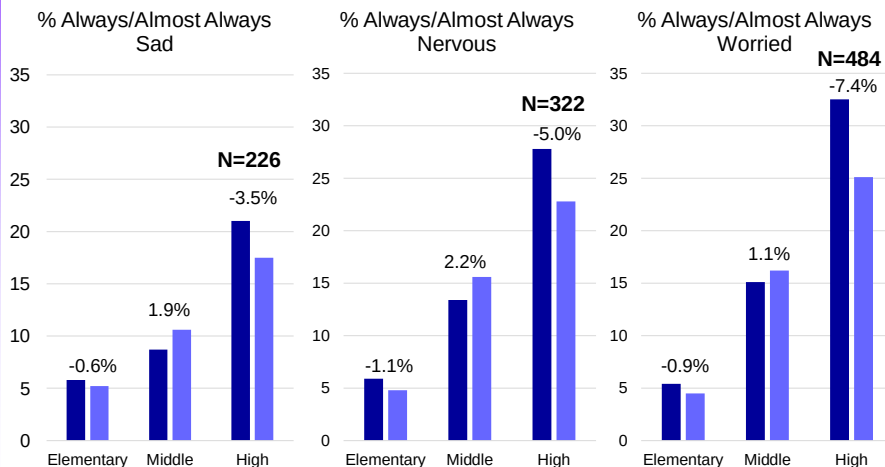
■ ES: +20 m, MS: -25 m, HS: -64 m



Sleep and Health Outcomes

Percent students reporting symptom in past 7 days

2017 2018





Goal SH-3: Increase the proportion of students in grades 9 through 12 who get sufficient sleep (8 or more hours of sleep on an average school night)

Sample	Baseline	Goal	Change
Healthy People 2020	30.9	33.1	+2.2



Goal SH-3: Increase the proportion of students in grades 9 through 12 who get sufficient sleep (8 or more hours of sleep on an average school night)

Sample	Baseline/2017	Goal/2018	Change
Healthy People 2020	30.9	33.1	+2.2
CCSD	26.8	57.7	+30.9

Earlier Parental Set Bedtimes as a Protective Factor Against Depression and Suicidal Ideation

James E. Gangwisch, PhD¹; Lindsay A. Babiss, BA²; Dolores Malaspina, MD³; J. Blake Turner, PhD⁴; Gary K. Zammit, PhD⁵; Kelly Posner, PhD⁶

Sleep (2011)

■ Nat'l Longitudinal Study of Adolescent Health

ODDS RATIOS (95% CI) FOR DEPRESSION		
Bedtime	Unadjusted	Adjusted
10 pm or earlier	1.00	1.00
By 11:00 pm	1.15 (0.94-1.40)	1.13 (0.90-1.42)

Earlier Parental Set Bedtimes as a Protective Factor Against Depression and Suicidal Ideation

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Sleep (2011)

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By 11:00 pm	1.15 (0.94-1.40)	1.13 (0.90-1.42)
By or after midnight	1.42 (1.21-1.67)	1.28 (1.07-1.52)

Earlier Parental Set Bedtimes as a Protective Factor Against Depression and Suicidal Ideation

James E. Gangwisch, PhD¹; Lindsay A. Babiss, BA²; Dolores Malaspina, MD³; J. Blake Turner, PhD⁴; Gary K. Zammit, PhD⁵; Kelly Posner, PhD⁶

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ODDS RATIOS (95% CI) FOR SUICIDAL IDEATION		
Bedtime	Unadjusted	Adjusted
10 pm or earlier	1.00	1.00
By 11:00 pm	1.15 (0.98-1.35)	1.15 (0.98-1.36)

Earlier Parental Set Bedtimes as a Protective Factor Against Depression and Suicidal Ideation

James E. Gangwisch, PhD¹; Lindsay A. Babiss, BA²; Dolores Malaspina, MD³; J. Blake Turner, PhD⁴; Gary K. Zammit, PhD⁵; Kelly Posner, PhD⁶

Sleep (2011)

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Bedtime	Unadjusted	Adjusted
10 pm or earlier	1.00	1.00
By 11:00 pm	1.15 (0.98-1.35)	1.15 (0.98-1.36)
By or after midnight	1.30 (1.13-1.49)	1.25 (1.07-1.45)

Future Direction #3

Nature vs. Nurture

- Need better understanding of unique genetic and non-shared contributions to sleep and developmental psychopathology
- Environmental factors, both within and beyond youth's control, contribute to sleep and daytime functioning
- Critical need to educate youth, families, and education systems about importance of sufficient sleep and healthy sleep habits

More Future Directions

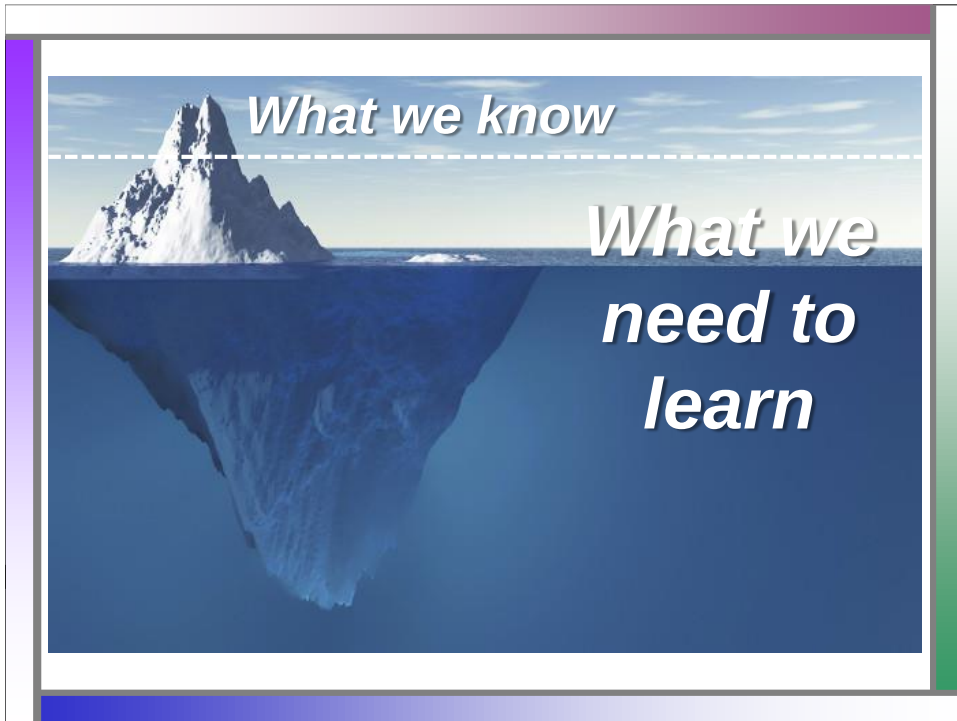
Future Directions in Sleep and Developmental Psychopathology

Lisa J. Meltzer

Department of Pediatrics, National Jewish Health JCCAP (2017)



- Role of night-to-night variability
- Contribution of circadian rhythm
- Individual vulnerabilities to sleep loss
- Treating comorbid sleep/psych issues
 - Transdiagnostic
 - Medications for sleep/psych



Sleep is a critical health asset, required for optimal health and well-being

Complex, bidirectional relationship between sleep and developmental psychopathology

Questions for today's talk

Developmental, sleep-related changes during sleep may assist with diagnosis and treatment

Both genetic and environmental factors contribute to sleep and psychopathology

Thank You!!



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National Jewish Health
meltzerL@njhealth.org

