

# Sleep during adolescence: Developmental changes and links to emotional function

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## Conflict of Interest Disclosures – Authors/Presenters

- The authors do not have any potential conflicts of interest to disclose,
- OR
- The authors wish to disclose the following potential conflicts of interest related to content in this lecture:

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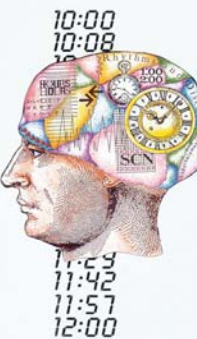
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### SLEEP



**Cognition**  
Think      Concentrate  
Learn      Remember  
Insight

**Emotion**  
Mood      Mental Health  
Stress     Social Interactions

**Behavior**  
Accidents   Motor Skills

**Health**  
Immune System  
Metabolism  
Insulin

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- 1. Sleep and psychiatric disorders: 2-way street
- 2. Epidemic of sleep deprivation in teens
- 3. Changes in sleep across adolescent development
- 4. Consequences of short sleep in adolescents
- 5. What can be done to improve adolescent sleep?
- 6. Experimental evidence: Sleep restriction effects on positive and negative affective systems

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### Sleep and psychiatric disorders: a 2-way street

- Sleep is disturbed in many psychiatric disorders, esp. those with core features of affect dysregulation.
- Sleep problems are a risk factor for developing psychiatric disorders, and associated with worse outcomes in patients with psychiatric disorders.
- Psychiatric symptoms and disorders are also overrepresented in sleep disorders.




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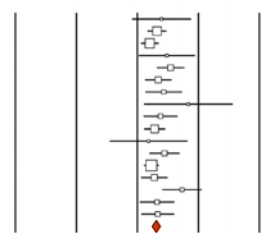
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### Meta-analysis of the effects of insomnia on future depression

Study name	Statistics for each study					Odds ratio and 95% CI
	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value	
Eschko-Cove et al 2010	2.49	0.83	7.48	1.62	0.10	
Kim et al 2009	2.10	1.48	2.97	4.20	0.00	
Bayliss et al 2008	1.80	1.16	2.71	2.95	0.00	
Cove et al 2008	3.05	1.07	8.72	2.68	0.04	
Jansson-Frigdmark & Lundbom 2008	3.51	2.11	5.83	4.84	0.00	
Risane & Taylor 2008	2.20	1.35	3.60	3.15	0.00	
Morphy et al 2007	2.71	1.37	5.37	2.86	0.00	
Petito et al 2006	6.86	1.30	36.14	2.27	0.02	
Hain et al 2003	2.40	1.28	4.51	2.72	0.01	
Ruberts et al 2002	1.82	1.30	2.83	3.30	0.00	
Johnson et al 2000	1.53	0.36	6.56	0.57	0.57	
Mallon et al 2000	2.78	1.59	4.88	3.58	0.00	
Foley et al 1999	1.70	1.29	2.24	3.80	0.00	
Chang et al 1997	1.90	1.16	3.10	2.57	0.01	
Wessman et al 1997	5.40	2.59	11.26	4.50	0.00	
Wessman et al 1996	2.10	1.10	4.00	2.25	0.02	
Vijlath et al 1989	2.16	1.17	3.99	2.48	0.01	

Fixed model Odds Ratio = 2.1 (1.9 – 2.4)

Baglioni, et al., *J Affect Disord*, 2011

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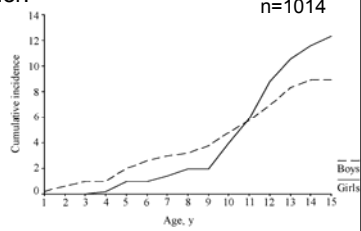
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### Insomnia increases during adolescence

- Community-based study of adolescents 13-16 years
- Lifetime prevalence 10.7%, with 53% comorbid with a psychiatric disorder.
- Rate increases over adolescence
- Onset of menses associated with 2.75 fold increased risk of insomnia



Johnson et al., 2006, *Pediatrics*

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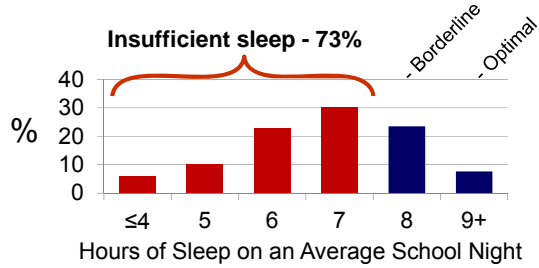
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### Epidemic of sleep deprivation in teens

- CDC - Youth Risk Behavior Survey (YRBS), 4 waves: 2007–2013
- n = 52,718 US high school students



Basch, et al. (2014). *Prev Chronic Dis*

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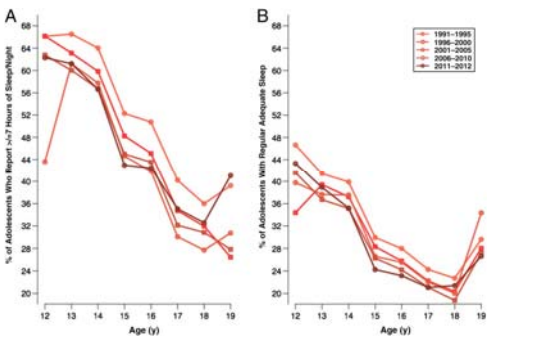
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### % with ≥ 7 hours sleep    % with adequate sleep



Keyes et. al (2015). *Pediatrics*.

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## Adolescent sleep changes

Sleep-wake characteristic	Change during adolescence
Sleep continuity/quality	Worsens (more insomnia)
Sleep duration	Decreases
Sleep timing	Shifts later
Daytime sleepiness	Increases



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Q: Why is short sleep so common in teens?

A: School / sleep squeeze

Result of unique **biological** and **social/environmental** influences during adolescence.

Biological changes begin post-puberty

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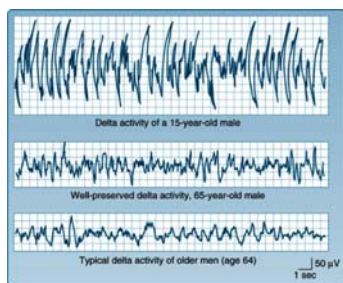
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## Adolescent sleep becomes lighter



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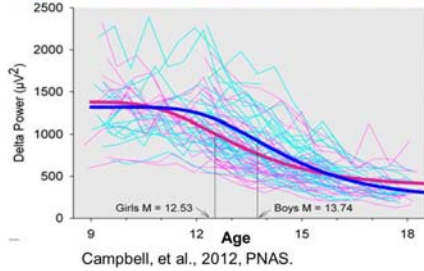
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## Adolescent sleep becomes lighter

### Slow wave sleep declines by 40%



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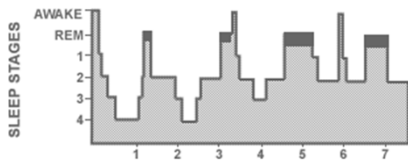
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## Rapid Eye Movement: REM Sleep



- Waking too early chops off morning REM sleep
- REM sleep is implicated in certain types of learning and memory, as well as creativity, and how we respond to emotional information

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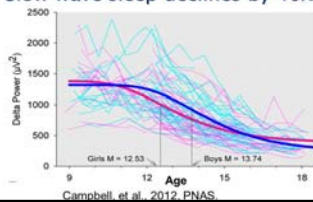
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## Why is short sleep so common in teens?

- School / sleep squeeze: Result of unique **biological** and **social/environmental** influences during adolescence.
- **Biological changes** in sleep at puberty:
  - Sleep becomes lighter (less homeostatic sleep drive)
  - Marked decrease in Slow Wave Sleep and delta power (Jenni, Achermann, & Carskadon, 2005).

### Slow wave sleep declines by 40%



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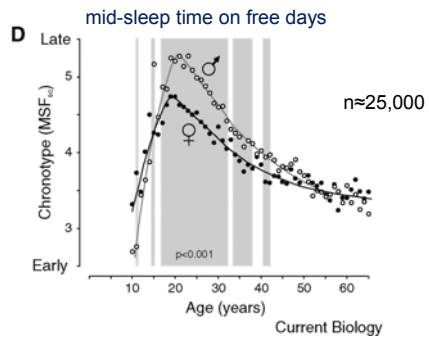
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## Sleep phase preference delays across adolescence



Cell Roenneberg, et al., 2004

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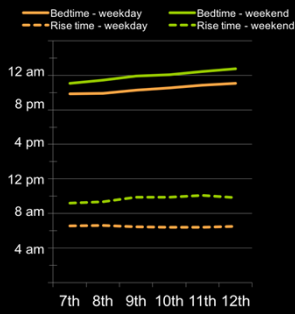
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## Adolescent sleep timing shifts later (delays)

### 2006 Sleep in America Poll



<https://sleepfoundation.org>

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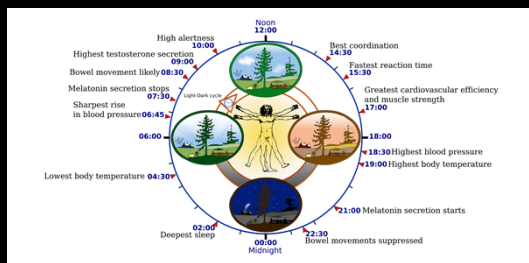
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## Circadian rhythms – (very brief) intro



- Organize physiological and behavioral processes for optimal interaction with the environment
- "Temporal order is essential for health" - Anna Wirz-Justice (2003)

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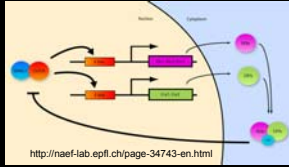
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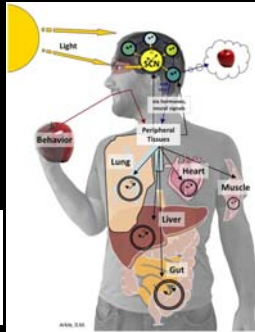
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## Circadian Rhythms: Clocks everywhere



<http://naef-lab.epfl.ch/page-34743-en.html>

Timing is everything: U.S. trio earns Nobel for work on the body's biological clock



Arble & Sandoval (2013) *Front. Neurosci*

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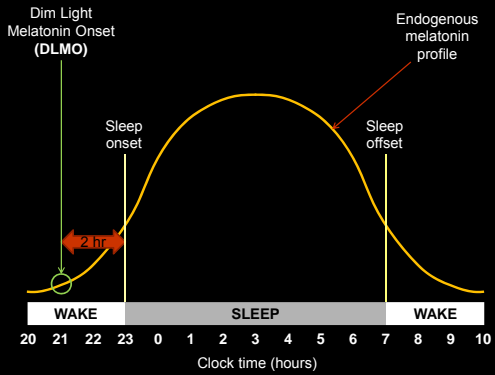
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## Measuring the clock with melatonin




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## Why is short sleep so common in teens?

- School / sleep squeeze: Result of unique **biological** and **social/environmental** influences during adolescence.
- **Biological changes** in sleep at puberty:
  - Sleep becomes lighter (less homeostatic sleep drive)  
Marked decrease in Slow Wave Sleep and delta power  
(Jenni, Achermann, & Carskadon, 2005).
  - Sleepiness increases
  - Circadian rhythms delay
    - Delayed melatonin onset (by ~ 2 h), leading to a tendency to prefer and have later bed and wake times
      - DLMO: Preschool ~ 7:30 PM
      - DLMO: Prepubertal ~8:30 PM
      - DLMO: Mature adolescents ~9:30 PM




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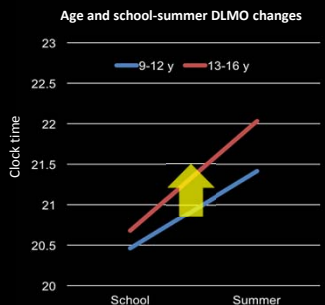
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## Adolescent circadian time shifts later (i.e., teens become biological night owls)



Crowley et al 2006 SLEEP

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## Circadian misalignment, defined

A mismatch between the timing of the behavioral sleep-wake schedule and that of the internal circadian clock




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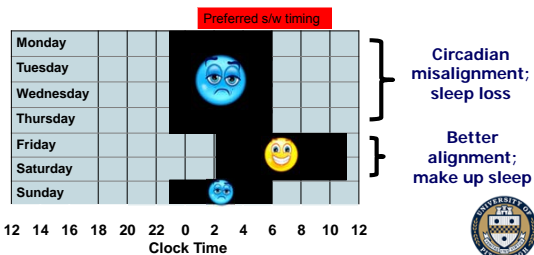
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## Delayed circadian timing during adolescence leads to chronic circadian misalignment

- Circadian and preferred sleep timing shift later (delay) during adolescence
- Mismatch with early school start times



Courtesy of Brant Hasler, PhD




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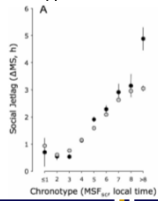
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## Social Jet Lag

- difference in sleep timing on school/work days and free days\*
- Very common pattern in adolescents
  - In 1,456 youth ages 11-17 from the NSF 2006 Sleep in America poll:
    - Weekend bed times were ~90 min later, ~75 min longer sleep than school days
    - At age 17, weekend bed times were 137 min later, with 93 minutes more sleep
- Tends to be worse for evening types/late chronotypes
  - ~1 hour weekend oversleep in morning larks
  - ~1.5 – 2 hours for intermediate types
  - ~3 hours weekend oversleep in night owls




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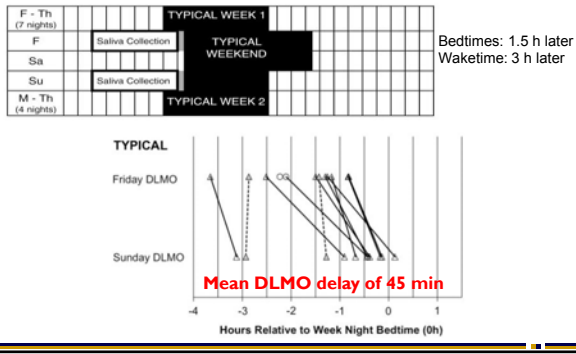
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## Social Jet Lag

- Melatonin onset (DLMO) in 12 teens ages 15–17 (Crowley & Carskadon, 2010)




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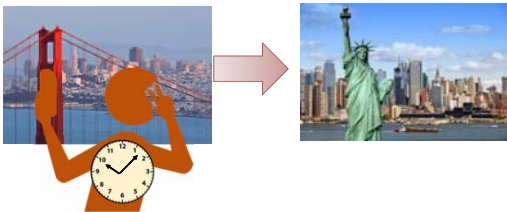
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## Social jet lag



Like traveling from SF to NYC every week...

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### Why is short sleep so common in teens?

- **School / sleep squeeze:** Result of unique **biological** and **social/environmental** influences during adolescence.
- **Biological changes** in sleep at puberty:
  - Sleep becomes lighter (less slow wave sleep)
  - Sleepiness increases
  - Circadian rhythms shift later (delayed melatonin onset)
- **Social / Environmental influences**
  - Decrease in parental control
  - Increase sensitivity to peers
  - Use of social media (texts, IMs, etc.) & exposure to light
  - Homework, after school work / activities
  - **Early school start times / transportation to school**

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### A growing list of organizations recommend starting middle/high school at **8:30am or later**

- American Academy of Pediatrics (AAP): August 2014
- Centers for Disease Control (CDC): August 2015
- American Medical Association (AMA): June 2016
- The Sleep Research Society (SRS)
- American Academy of Sleep Medicine (AASM): April 2017
- The National Association of School Nurses
- **2017: Society for Behavioral Sleep Medicine (SBSM)**
- **The National Education Association (NEA)**
- **National Parent Teacher Association (PTA)**
- And others....

[Let Them Sleep: AAP Recommends Delaying Start Times of Middle and High Schools to Combat Teen Sleep Deprivation](#)

8/25/2014

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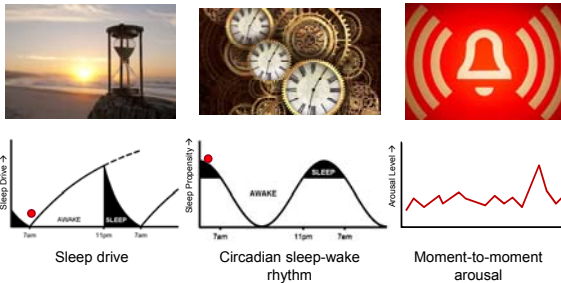
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### What controls sleep? The hourglass, the clock, and the alarm

How long you've been awake      Time of day      Level of arousal



Courtesy of Daniel Buysse, MD

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### What happens in adolescence?


How long you've been awake

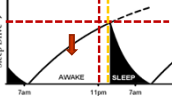


Time of day

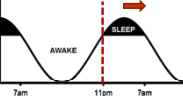


Level of arousal

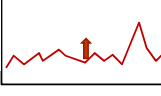




Sleep drive: **Takes longer to build up**



Circadian sleep-wake rhythm: **Later timing**



Moment-to-moment arousal: **Increases**

Courtesy of Daniel Buysse, MD

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### Consequences of short sleep: Physical health

- Overweight/obesity
  - Link between short sleep and overweight, obesity in middle school, high school
- High blood pressure and diabetes linked to short sleep duration
- Impairs immune function, and thus, healing and recovery
- Short sleep duration in adolescence in girls predicted increased risk of high cholesterol as a young adult ([Gangwisch, et al., 2010, SLEEP](#))



Shochat et al., 2014, Sleep Med Reviews

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### Consequences of insufficient sleep in adolescents

- Increased sports-related injuries
  - 7<sup>th</sup>-12<sup>th</sup> graders in California school (Milewski, et al., 2012 abstract)
  - Those who slept 8+ hours were 68% less likely to be injured
  - Risk also increased for higher grade level
    - Independent of gender, amount of sports participation per year, # of sports, strength training



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### Consequences of insufficient sleep in adolescents



- **Motor Vehicle Accidents**
  - Leading cause of death in teenagers (CDC, 2012)
    - In 2010, 22% of drivers ages 15–20 had been drinking
  - Teen drivers ages 16–19 are 3x more likely to be in a fatal crash vs. drivers 20+
  - Teen drivers are at the **highest risk** of car accidents due to falling asleep, accounting for 50% of all crashes
  - NSF poll (2006): 68% of HS seniors reported driving while drowsy; 15% at least a week

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### Consequences of insufficient sleep in adolescents

- **Mood**
  - Greater depressive symptoms (Pasch et al. 2011; Roberts & Duong, 2014); suicidal ideation, attempts, and death (Goldstein et al. 2008; Wong et al. 2012)
- **Increased substance use**
  - Short sleep is associated with more caffeine, smoking, alcohol, substance use, and stimulant abuse (McKnight-Eily, et al. 2011; Hasler et al. 2017; Terry-McElrath et al., 2017)
- **Increased risk taking behavior**
  - Violence, unsafe behaviors, drug use and sexual activities more common in short sleepers (O'Brien & Mindell, 2005; Owens et al., 2017)
- **Delinquent behavior**
  - Short sleep duration and delayed bedtimes were directly associated at age 16 (but not ages 22 or 28) in National Longitudinal Study of Adolescent Health (Peach & Gaultney, 2013)
    - Partly mediated by increased sensation seeking and reduced impulse control

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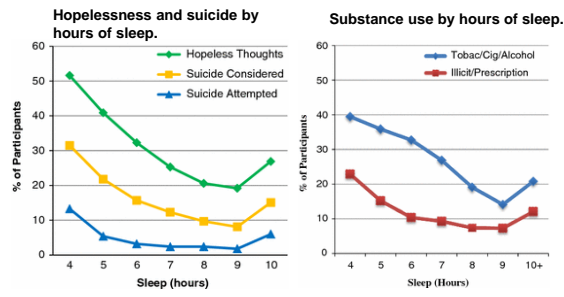
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### The “dose” of sleep loss increases negative consequences: Fairfax County VA (n=27,939)

Winsler, et al. 2015, *J Youth Adolesc*



Note: Each hour less of sleep is associated with a significant increase in odds of the outcome, p's < .001

Winsler, et al. 2015. Journal of Youth and Adolescence

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### Consequences of insufficient sleep in adolescents

- Depression
  - n > 3,000 followed for 1 year from Teen Health 2000 (Roberts & Duong, *Sleep*, 2014)
  - ≤ 6 h sleep on weeknights
    - ~20% at wave 1
    - ~25% at wave 2
- Sleep and depression associated at baseline
- Short sleep at baseline increased risk at follow up:
  - Depressive symptoms: increased 25-38%
  - Depression: by a factor of > 3 (Odds ratio: 3.12, 95% CI: 1.6–6.3)

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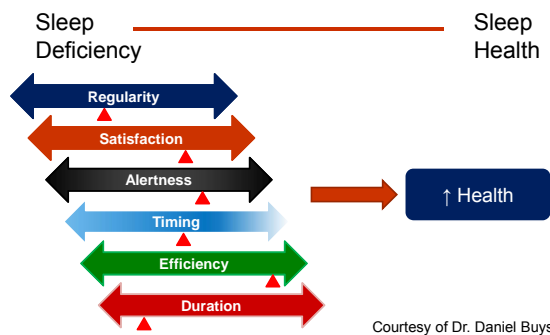
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Sleep health is a multidimensional pattern of sleep-wakefulness, adapted to individual, social, and environmental demands, that promotes physical and mental well-being.




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### Sleep health and health risk in adolescents



- 176 adolescents (mean 14.8 yrs, 58% F)
- At risk for poor health outcomes
- Predictor: Sleep health "good" or "poor" on 6 self-report dimensions (RU\_SATED)
- Outcome: Composite health risk for emotional, cognitive, behavioral, social, physical health

Dong, Martinez, Buysse, Harvey, *submitted*.

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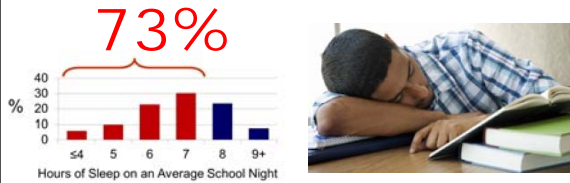
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- Adolescent (and adult) sleep deprivation is a widespread, chronic health problem
- ...and is associated with negative outcomes.
- So, what can be done to improve sleep health, and perhaps prevent socio-emotional problems?




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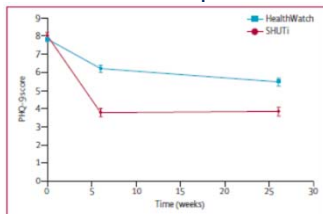
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### CBT-I reduces depressive symptoms in individuals at risk for depression



- N = 1149 Australian adults
- At risk for depression based on depressive symptoms
- Outcomes: Depressive and other symptoms, depression dx
- Follow-ups at 6 weeks, 6 months

Christensen, *Lancet*, published online January 27, 2016 [http://dx.doi.org/10.1016/S2215-0366\(15\)00536-2](http://dx.doi.org/10.1016/S2215-0366(15)00536-2).

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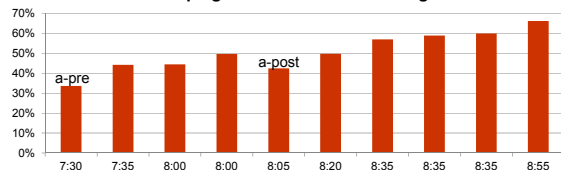
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### The case for later school start times

- Wahlstrom (2014): 3-year CDC-funded study
  - n=9,089 students in 8 public high schools in three states, most of which had already shifted school start times later by 30 to 60 minutes.



- Teens who got < 8 h of sleep**
  - Higher depression symptoms
  - Greater caffeine
  - More substance use
- Teens with school starts later than 8:30 AM**
  - Higher grades in core subject areas
  - Higher state and national achievement tests
  - Higher attendance rates
  - Reduced tardiness

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## The case for later school start times: Narrowing the achievement gap

- A recent review (Wheaton, Chapman, Croft, 2016) of 38 studies found that later start times are associated with:
  - Higher attendance
  - Reduced tardiness
  - Reduced drop-out rates
  - Improvements in standardized test scores
  - Better grades
  - Involvement in extra-curricular activities remains the same or increases
- Disadvantaged students and highest achieving both benefit.
  - In one study, SAT scores for top 10% of students increased > 200 points with later start times.
  - "Early school start times reduce performance among disadvantaged students by an amount equivalent to having a highly ineffective teacher." Jacob & Rockoff, 2011, Brookings Institute Report

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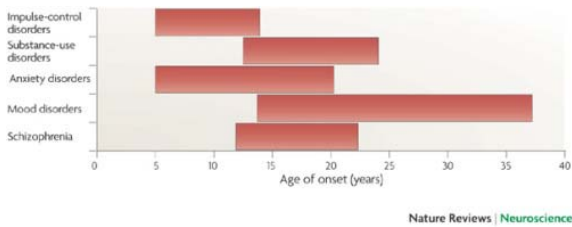
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## Adolescence: A period of vulnerability that may be further exacerbated by sleep loss



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## The sleepy brain & the health paradox of adolescence



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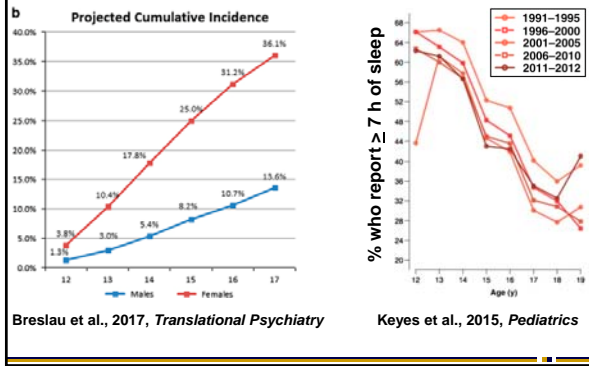
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## Sleep loss and depression are both extremely prevalent during adolescence




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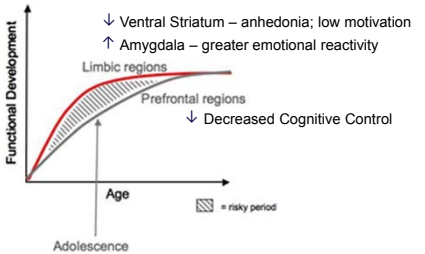
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## Adolescence: A period of vulnerability that may be further exacerbated by sleep loss



Casey, Jones, & Hare (2008). *Annals of the New York Academy of Sciences*, 114.

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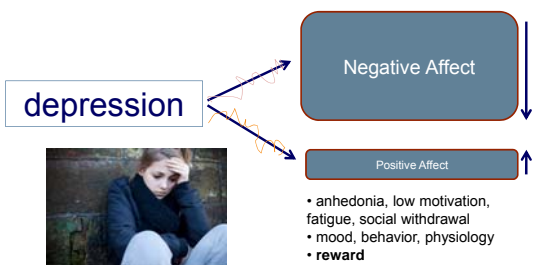
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## Depression and Affect Regulation



Forbes & Dahl, 2005, *Development and Psychopathology*; Forbes & Dahl, 2012, *JCPP*; Gross & Muñoz, 1995; Mayberg, 2003; Phillips, Drevets, Rauch, & Lane, 2003; Clark & Watson, 1991; Fowles, 1994; Hasler et al., 2004; Forbes & Dahl, 2005; Davey, Yücel, & Allen, 2008; Treadway & Zald, 2011

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### Within-subjects crossover design: Two 48-hour laboratory visits

**SLEEP EXTENSION**

10:00 pm	10 h in bed	8:00 am	10:00 pm	10 h in bed	fMRI	8:00 am
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**SLEEP RESTRICTION**

1:00 am	4 h	5:00 am	1:00 am	4 h	fMRI	5:00 am
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- n=48 Healthy adolescents in 6<sup>th</sup> – 8<sup>th</sup> grade, ages 11.5 – 15.0, completed both experimental sleep conditions.
- n=37 with fMRI data:
  - Reward processing: Event-related card guessing task to separate out anticipatory (liking) and consummatory phases
  - Explicit emotion regulation task (cognitive reappraisal)

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### The Reward Circuit

**Blunted striatal response to reward during adolescence:**

- Increasing depressive symptoms (Hanson et al., 2015; Morgan et al., 2013; Stringaris et al. 2015);
- offspring of mothers with a history of depression (Sharp et al., 2014);
- currently depressed youth (Forbes and Dahl, 2012; Stringaris et al. 2015);
- poorer response to depression treatment (Forbes et al., 2010a);
- shorter sleep duration (Holm et al., 2009);
- variable sleep timing (Hasler et al., 2012)

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### Monetary Reward Task - Event Related Design

Guess	Anticipation	Outcome	Baseline
?	Poss. WIN ↑	+	
< or > 5	Poss. LOSS ↓		
4 s	6 s	1 s	6 s
			3 s

Magnitude: 2 conditions		Outcome	
	Low	High	
Win	\$1	\$10	Win No win
Loss	-\$0.50	-\$5	Loss No Loss

Ans. 2

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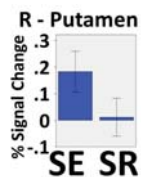
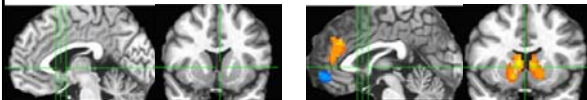
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**Sleep restriction blunts striatal response to reward outcome (winning \$10):**

SLEEP RESTRICTION (SR)

SLEEP EXTENSION (SE)




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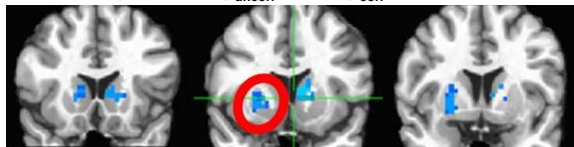
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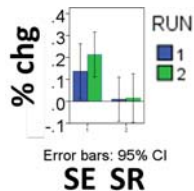
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**Sleep Restriction Effect: Reward Outcome**

Paired samples t-test:  $p_{uncorr} < .005$ ,  $p_{corr} < .05$



- most evident in youngest participants ( $r=0.35$ )
- outcome only
- high magnitude only




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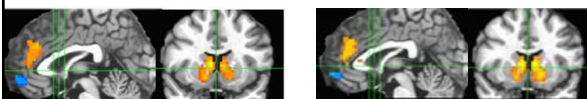
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**Intact striatal responses during reward anticipation (hoping to win \$10):**

SLEEP RESTRICTION (SR)

SLEEP EXTENSION (SE)



Equivalent activation across SR & SE (no paired sample differences) suggesting an intact wanting system.

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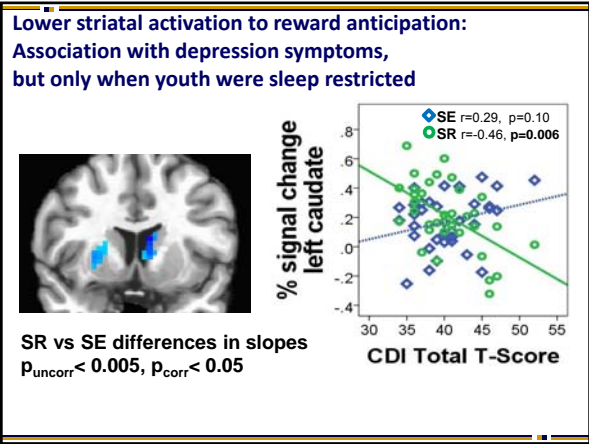
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## Slide 56

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- FP1** ERIKA - here's an alternative reward outcome slide. Please note: The bar graph below shows that there was not habituation between T1 and T2 that were impacting sleep condition-related effects (which was not true for the low-magnitude rewards, where both conditions were habituated at T2 for anticipation.)  
Franzen, Peter, 11/30/2017
- FP2** Also, this version contains the paired-sample t-test maps, which may not be necessary.  
Franzen, Peter, 11/30/2017




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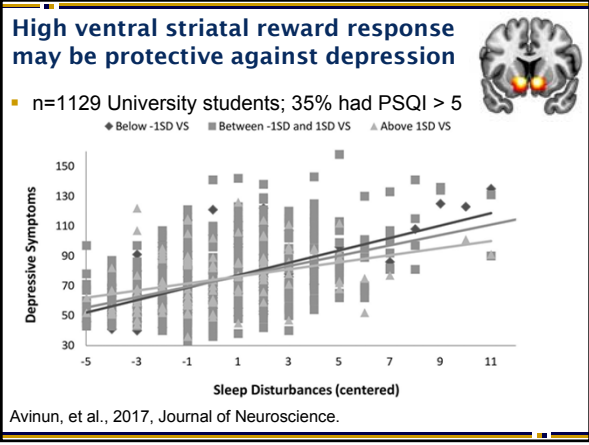
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**Positive affective systems: Summary**

- Acute sleep restriction in middle school students alters striatal responses to high-magnitude rewards.
  - Blunted striatal activity to receipt of rewards
  - Similar striatal activity during reward anticipation, but negatively associated with depressive symptoms and resilience to mood deficits when sleep restricted.
- Opposite findings observed following 1 night of acute sleep restriction (~4 hrs) in healthy young adults on the same task.
- Chronically insufficient sleep may alter the development of neural reward circuitry more substantially, leading to problems such as depression.

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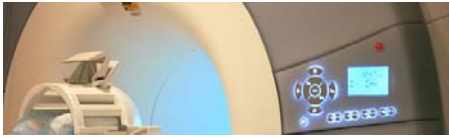
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## How does sleep loss impact the ability to down-regulate emotional responses?

Unconscious, effortless, & automatic

Conscious, effortful, & controlled / voluntary




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## Explicit (Voluntary) Emotion Regulation

- Task involves processing stimuli under 2 conditions:
  - 1) Instructed to react naturally
  - 2) Instructed to regulate emotional responses
    - Reappraisal: Change the way they think about the stimuli in order to reduce negative feelings
- Participants given ample opportunity to practice
- Explicit emotion regulation performance is indexed by contrasting emotional responding in the reactivity and regulation trials.

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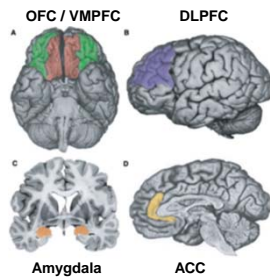
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## Explicit Emotion Regulation Task

- Explicit emotion regulation strategies can reliably influence emotional responding
  - Both self-report, and peripheral physiology
- Imaging findings:
  - Increases in areas associated with non-emotional forms of cognitive control
    - VLPFC, DLPFC, DMPFC
  - Decreases in limbic regions
    - Amygdala, insula




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### Emotion Regulation Task

2 sec Instructional Cue	8 sec On-line Regulation	4 sec Emotion Rating	6 sec Rest before next trial
Decrease or Look	Negative or Neutral IAPS Photos	How negative do you feel? 1...2...3...4...5 Not At All      Very Much	Relax

**Look: Attend to picture stimuli (i.e., passive viewing)**

- 20 neutral picture trials
- 20 negative picture trials

**Decrease: Use cognitive reappraisal to down-regulate emotional response**

- 20 negative picture trials

The 60 trials were presented in a fixed, psuedo-random order.

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### Emotion Regulation: Decrease negative vs. passive view negative pictures

DLPFC (BA 9 & 46): SR < SE p<0.001

**Sleep Restriction**      **Sleep Extension**

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### Auditory Valence Identification Task

IADS: International Affective Digitized Sounds  
42 trials (14 / valence) randomly presented

**ONE TRIAL**

\* Baseline pupil size (just prior to cue onset) is subtracted to examine mm change in pupil diameter (i.e., baseline corrected waveforms).

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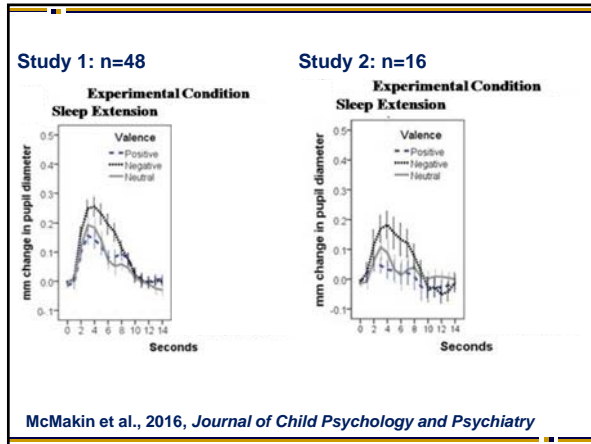
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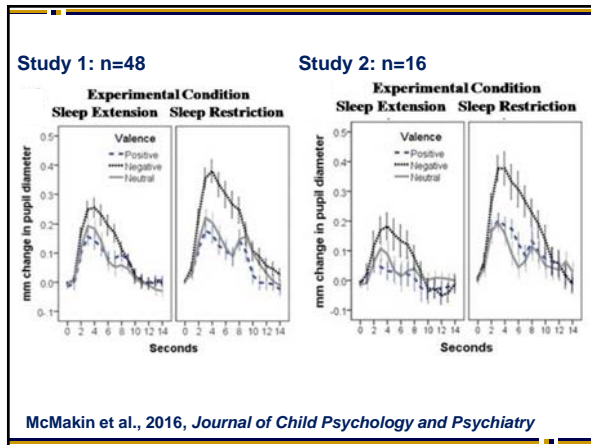
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**Effect of sleep restriction on peer interactions**

- Affective behavior during (dyadic) peer interactions in adolescents
  - Interpersonal context primed for negativity: discuss conflict
- Interactional Dimensions Coding System-Revised
  - Macro-analytic coding of negative & positive affective behaviors (observable behavior, facial expressions, and verbal content)
    - Positive behaviors
      - Positive affect, problem solving, support validation
    - Negative behaviors
      - Negative affect, dominance, conflict, and withdrawal

$F_{1,15}=5.45, p=0.03$

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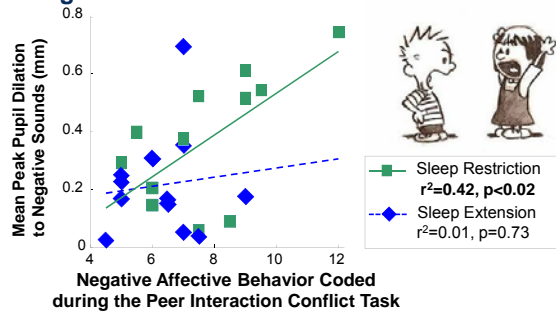
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**Pupillary reactivity to negative sounds is associated with observed negative behaviors during the conflict discussion**



McMakin et al., 2016, *Journal of Child Psychology and Psychiatry*

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**Negative affective systems: Summary**

- Sleep restriction may impair the ability to regulate emotional responses.
- When sleep restricted, adolescents displayed greater reactivity to negative stimuli.
- Blunted activity in regions involved in the cognitive control of emotion.
- More negative affect was observed during a conflict task.

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**Future Directions**

- We need to further understand the mechanistic relationship between sleep and emotion.
  - How much sleep loss leads to affective dysregulation?
    - Acute vs. chronic sleep loss
  - How does this unfold across development?
    - Is there an inflection point when sleep loss has the largest effects?
    - Do these sleep-brain associations predict the development of psychopathology?
  - Sleep loss versus sleep disturbance
    - How do various domains of sleep health (regularity, timing, quality) contribute to abnormalities in affective circuitry?
    - Would increasing sleep or treating sleep disturbances, such as insomnia, normalize the brain network underlying positive or negative affective systems?

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## Acknowledgements

### Collaborators:

- Daniel J. Buysse, MD
- Ronald E. Dahl, MD
- Erika E. Forbes, PhD
- Neil P. Jones, PhD
- Greg J. Siegle, PhD

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- University of Pittsburgh Clinical and Translational Science Institute

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- Sarah Gratzmiller
- Beth Hafer, MEd
- Denise Duryea

### Sleep Lab Staff:

- Christina Nicassio
- David Cashmere
- + sleep techs

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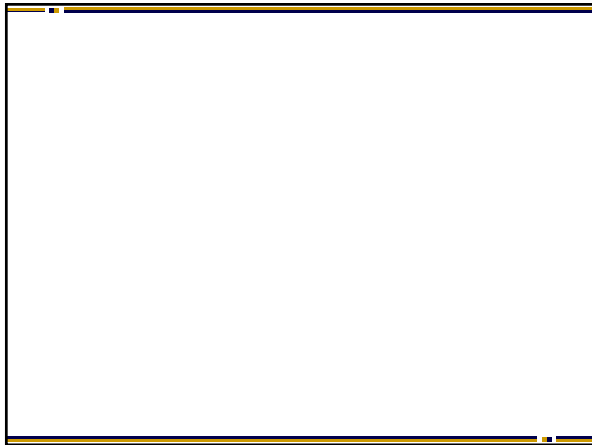
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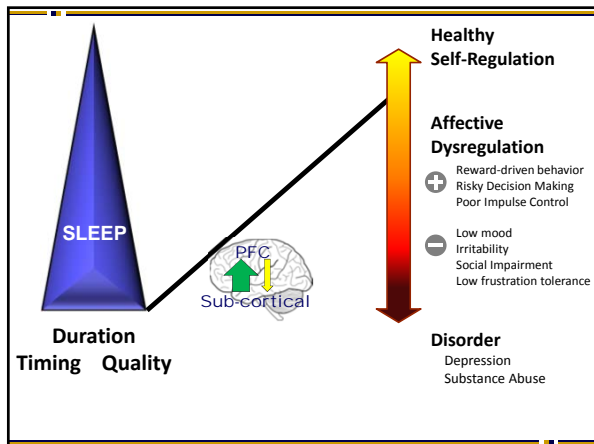
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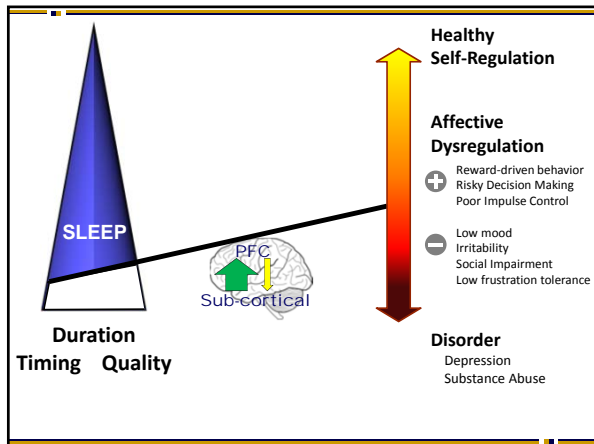
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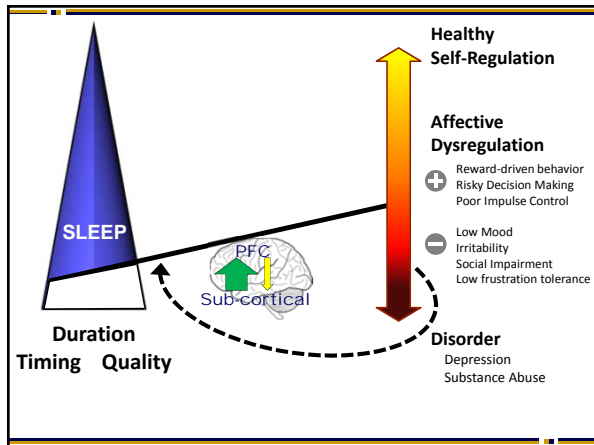
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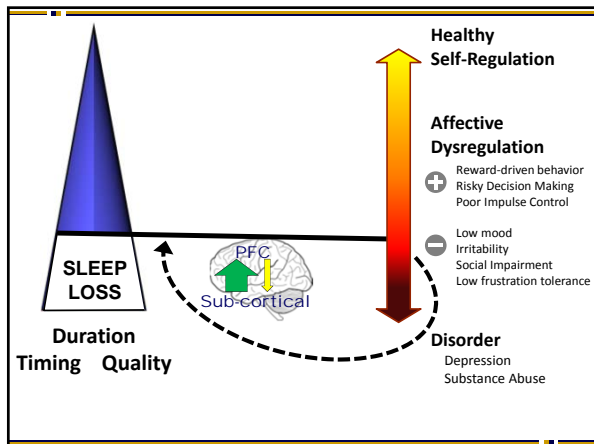
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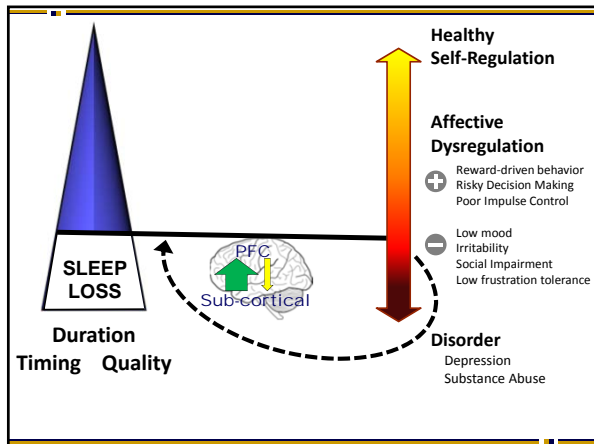
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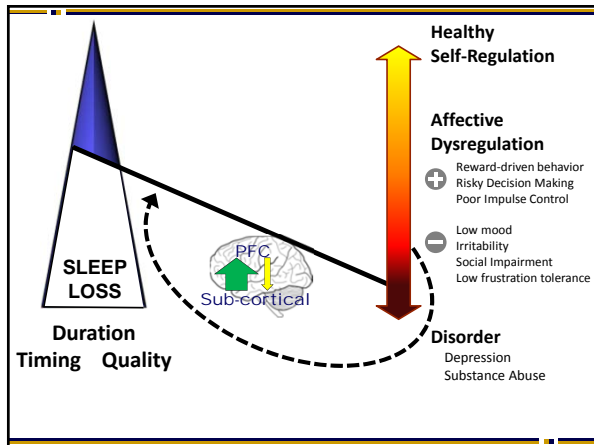
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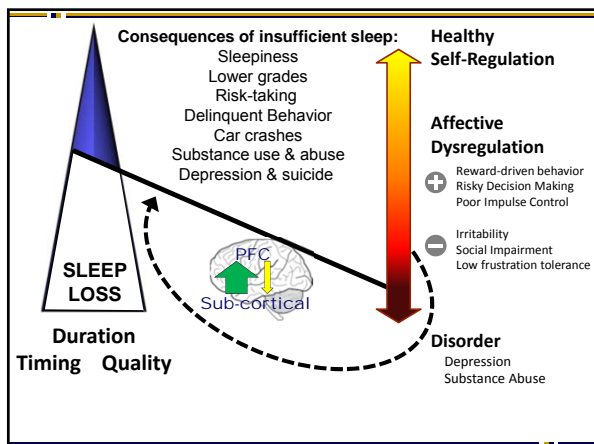
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**Development of the reward system during adolescence**

- Prefrontal cortical regions and striatum continue to develop during adolescence
- Two opposing views for what drives adolescent reward-seeking and risk taking:
  - Striatum is hypo-reactive during adolescence, leading to increased sensation-seeking
  - Striatum is hyper-reactive during adolescence
- How does sleep loss impact neural responses to reward during adolescence?

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