Doing Well By Sleeping Less ?
Things You Suspected About Sleep Deprivation But Were Afraid To Ask

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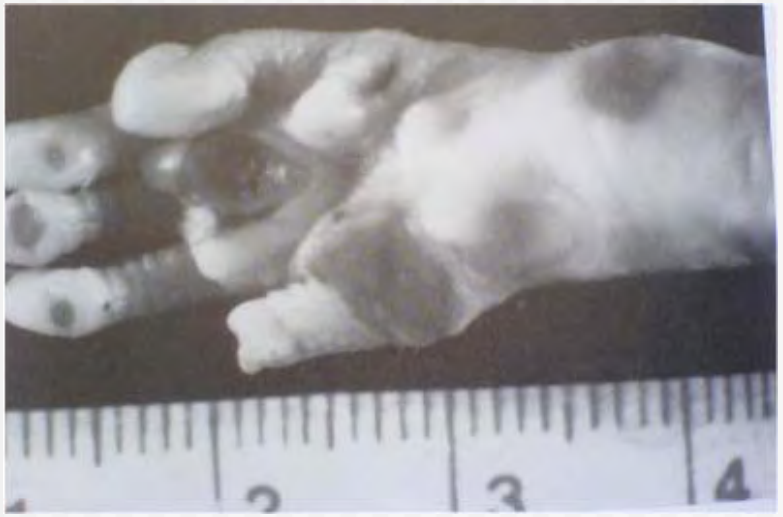
Outline

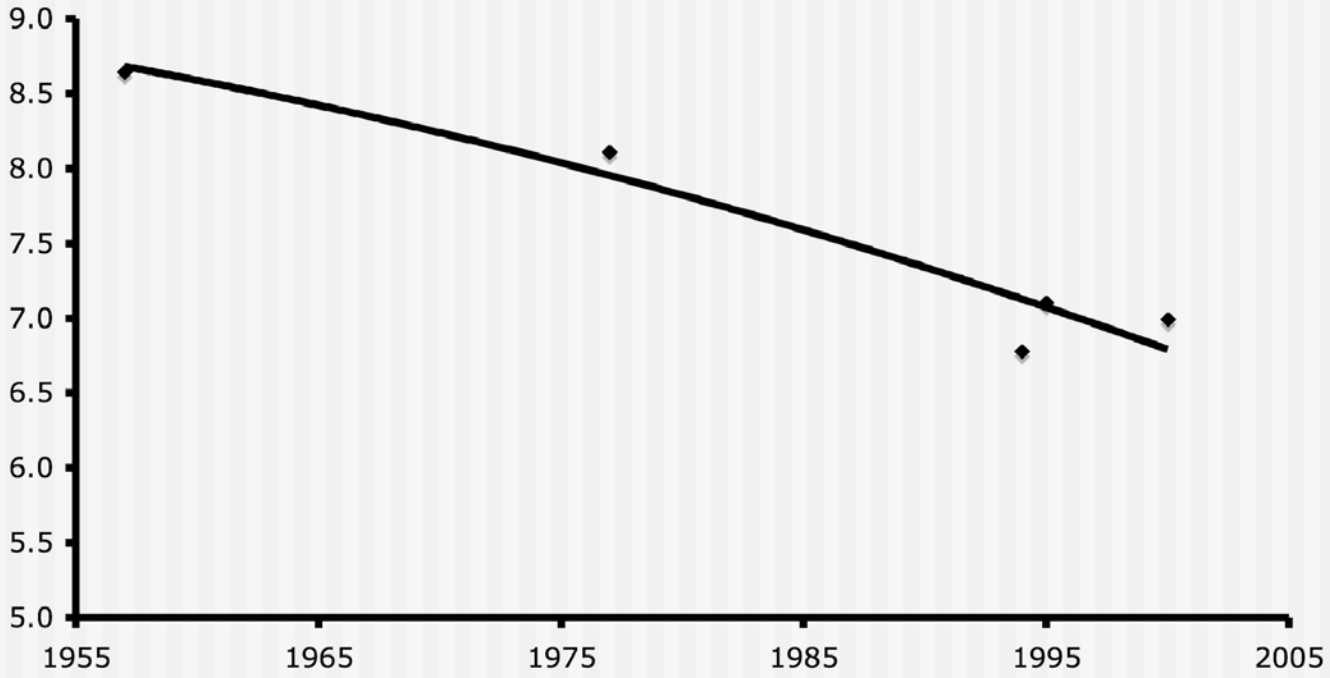
- Why do we sleep?
- Contexts under which sleep deprivation occurs
- Cognitive effects
- Cardiovascular effects
- Endocrine and metabolic effects
- Countermeasures

Why Do We Sleep?

Effects of 27 Days of Sleep Deprivation on a Rat



Self reported sleep duration in the US from 1960-2002



NSF Sleep in America Poll 2001-2002

Contexts in which sleep deprivation occurs

- Well persons
  - No choice
  - Have choice
- The Sick
  - Chronic pain
  - Sleep disorders

Contexts in which sleep deprivation occurs

- Total sleep deprivation
  - Intense military missions
  - Health care workers going on call
  - Lifestyle choices e.g. video game, gambling addiction
- Sleep fragmentation
  - Aging, OSA, PLMD
  - Shift work
- Chronic sleep restriction
  - High pressure work schedules
  - Lifestyle choice
  - Insomnia

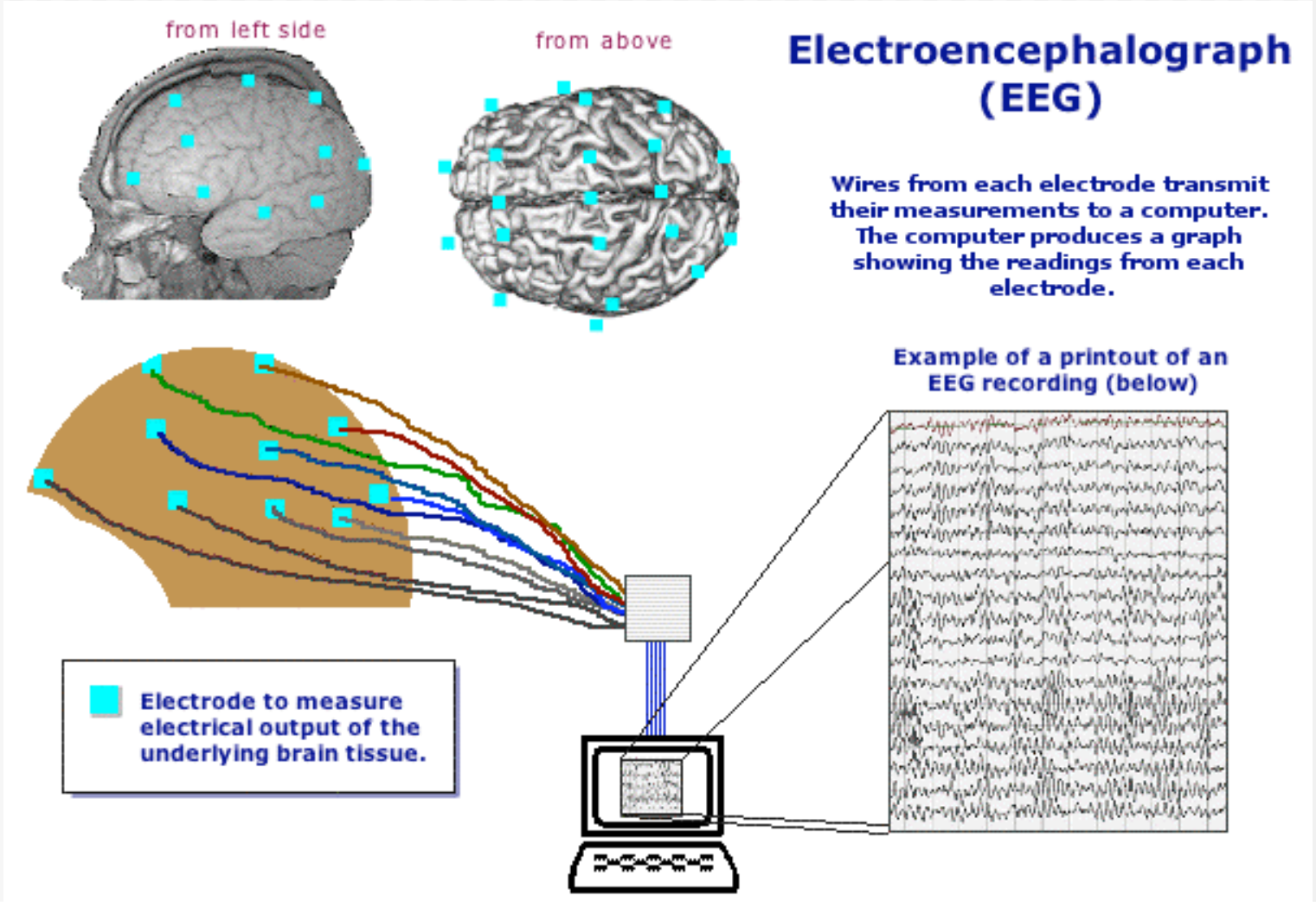
Sleep and Wakefulness Are Distinct

Sleep Involves

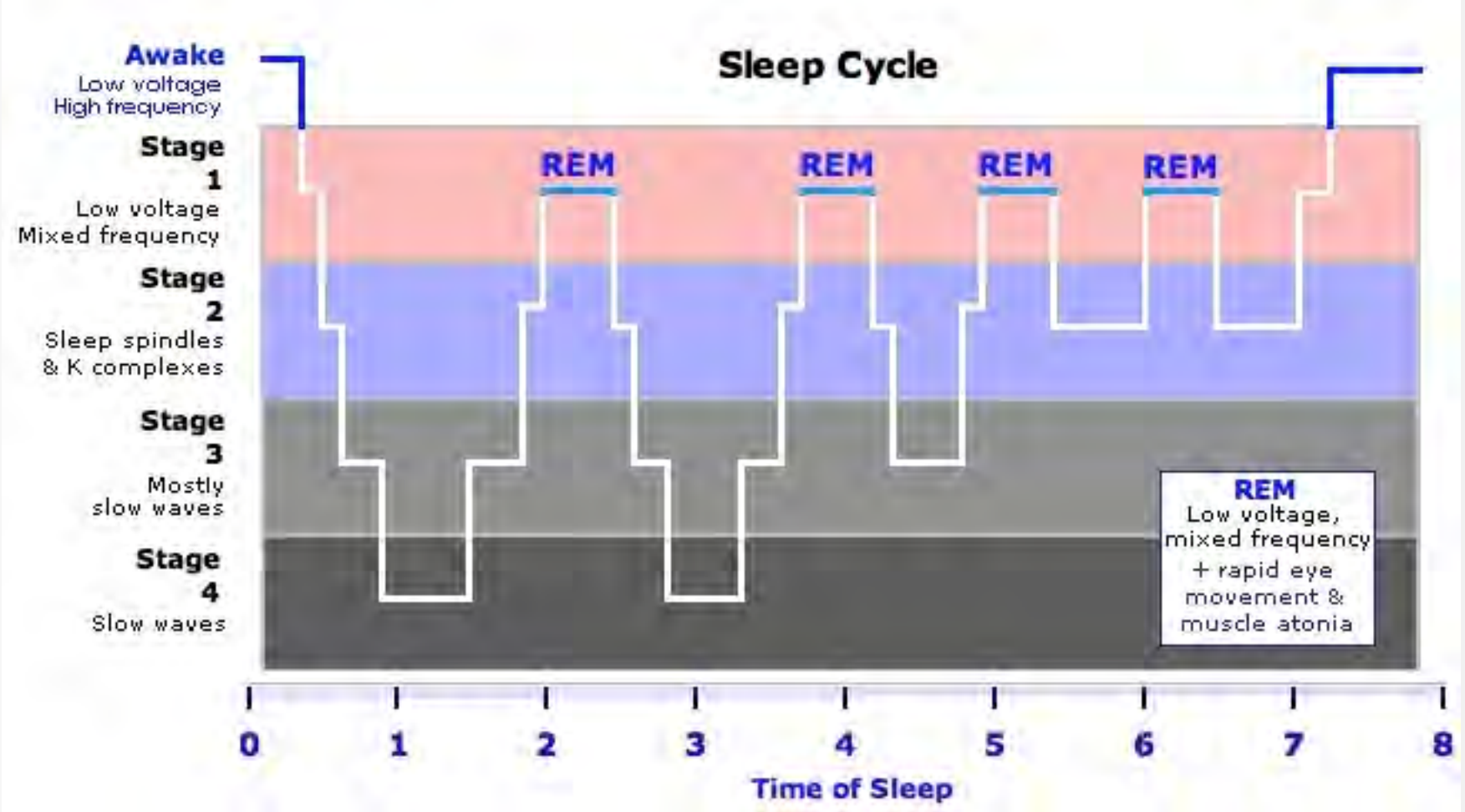
- Changes in posture and muscle tone
- Reduced physical activity
- Reduced level of arousal or responsiveness to sensory stimuli
- Easy reversibility of latter (relative to coma, stupor, hibernation)

Rechtstaffen & Siegel 2000

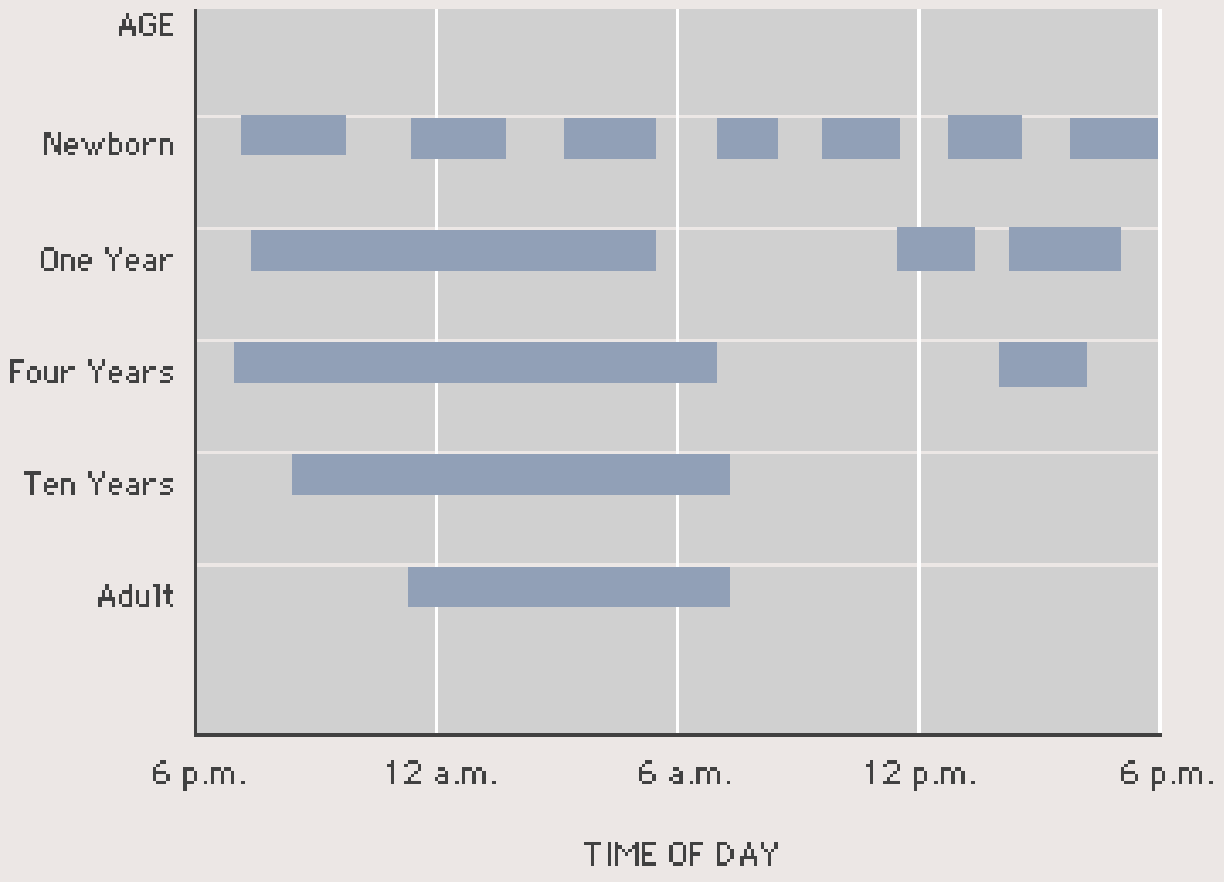
Sleep is objectively measured using EEG



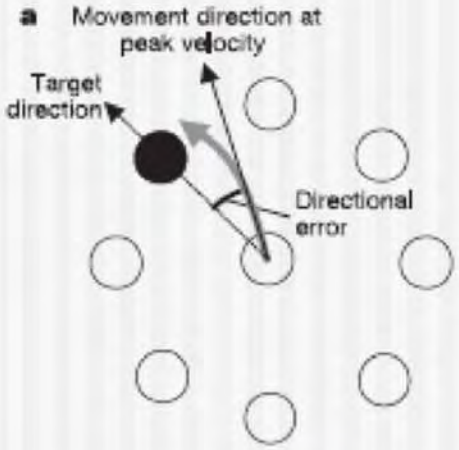
Normal Sleep Architecture In A Young Adult

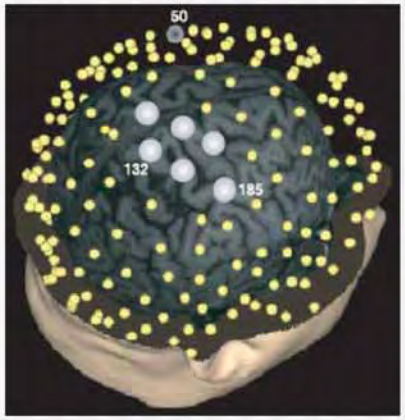


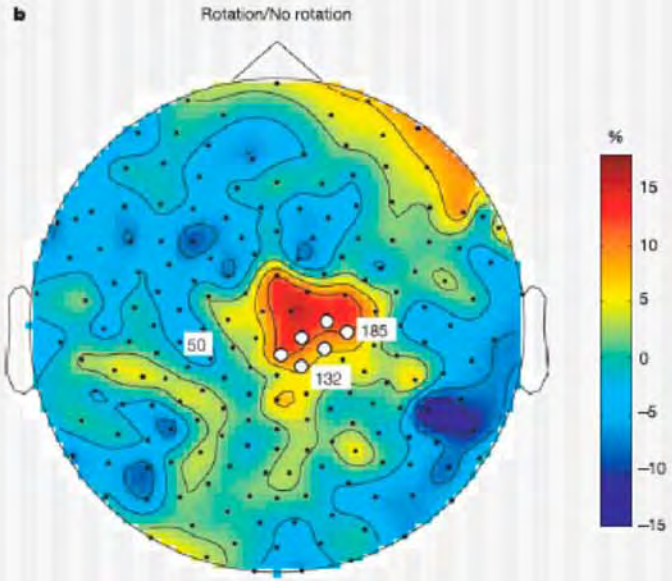
Sleep structure changes through one's lifetime



Learning Induces Brain Changes That Affect Subsequent Sleep

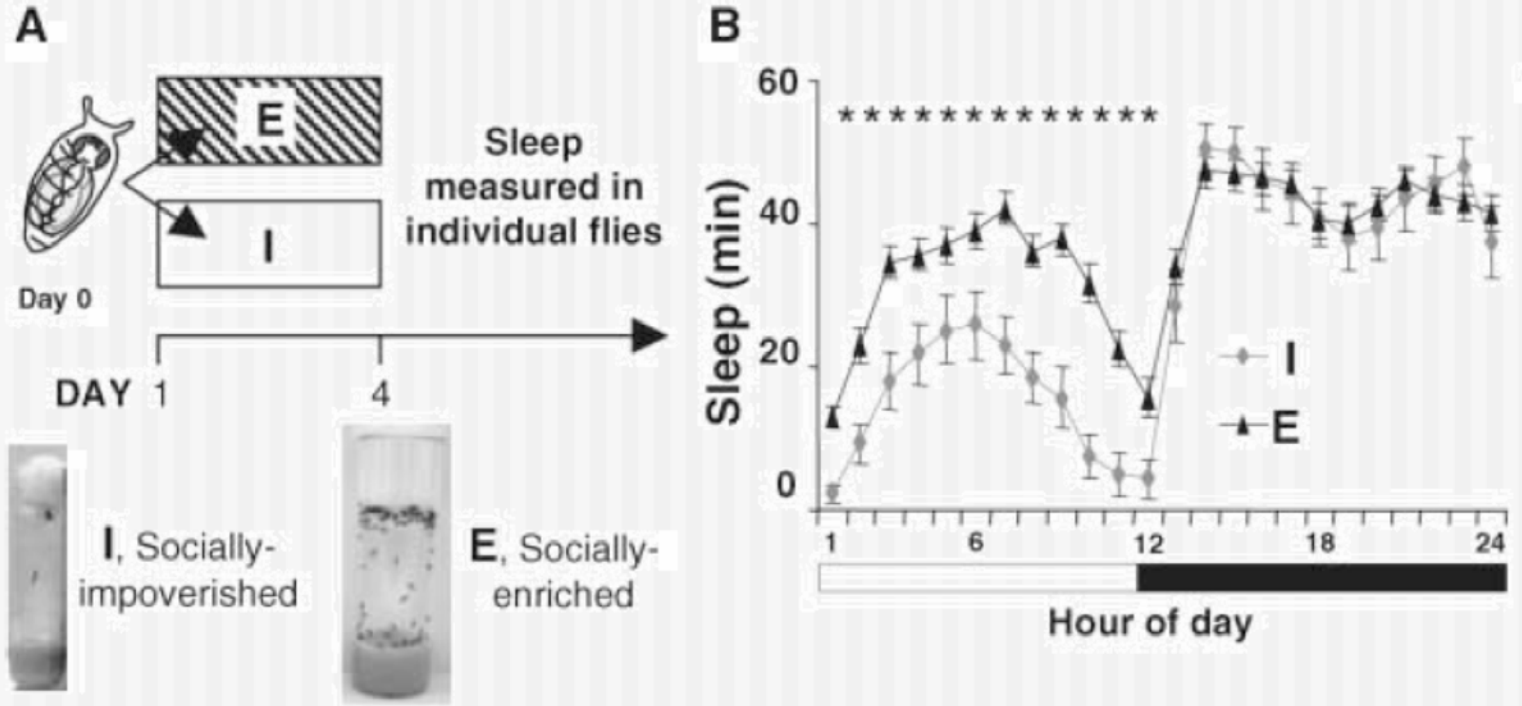






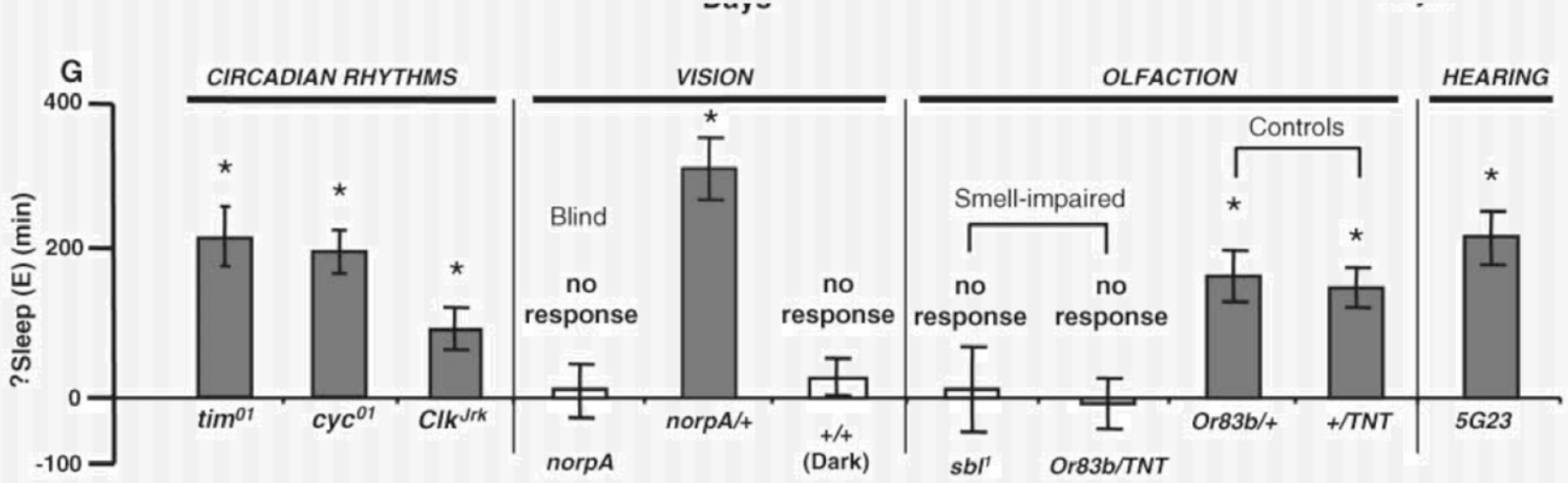
Huber Nature (2004)

Waking experience increases sleep need … in flies



Ganguly-Fitzgerald, Donlea, Shaw: Science (2006)

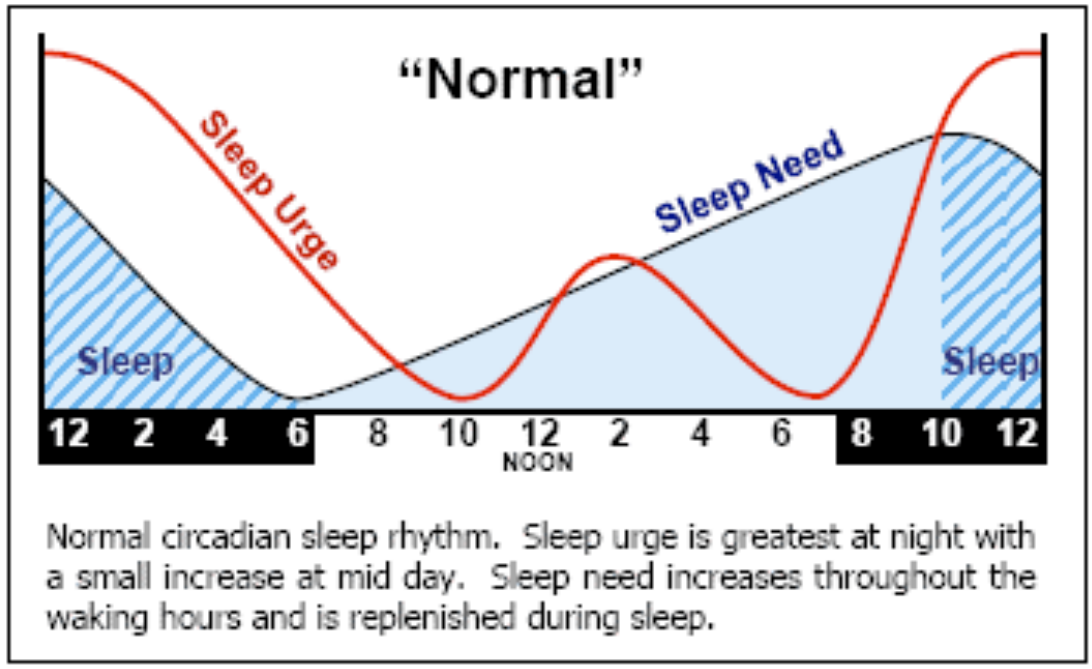
Waking experience … tied to sensory stimulation



Ganguly-Fitzgerald, Donlea, Shaw: Science (2006)

Processes regulating normal sleep

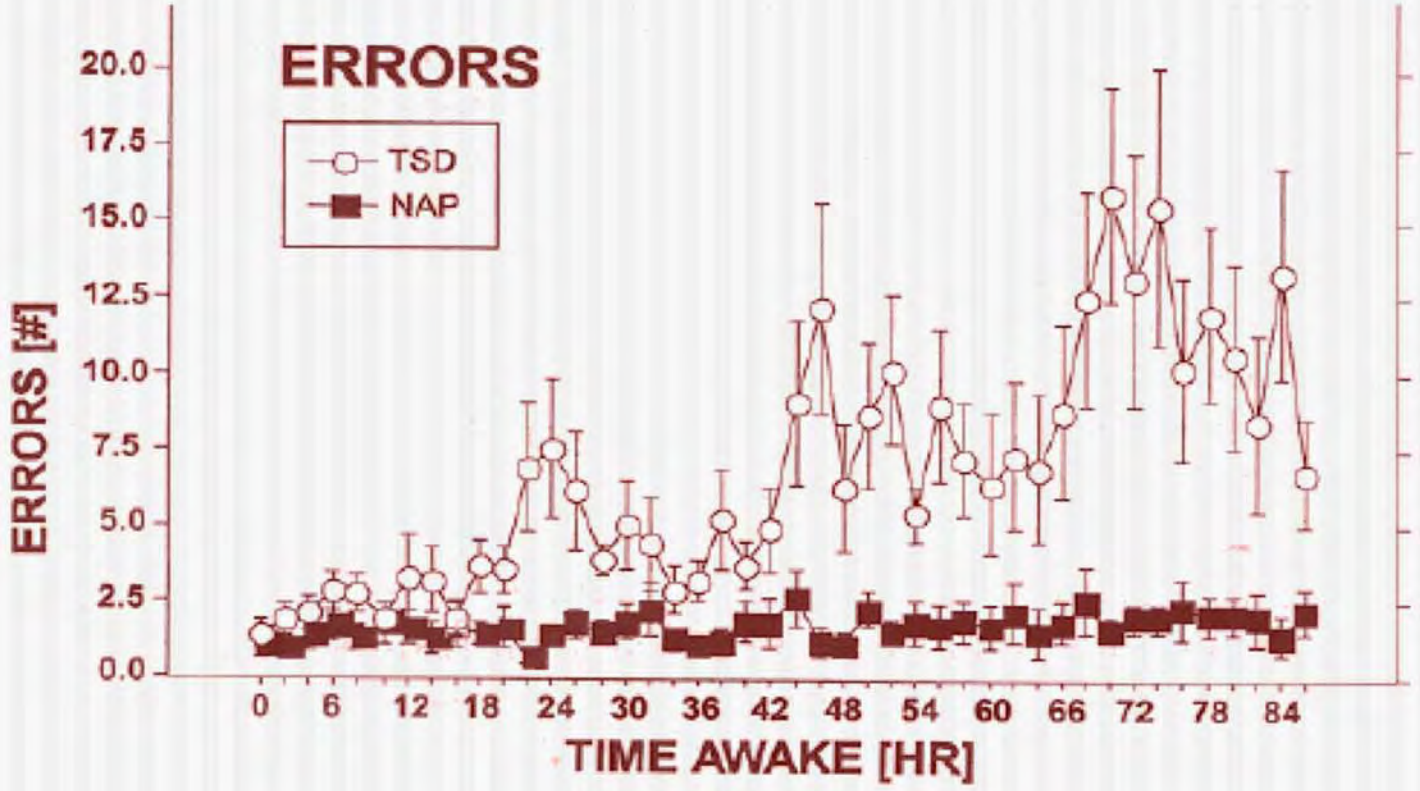
- Cyclically varying circadian influence: Process C
- Gradually increasing effect of time awake: Homeostatic effect; Process S



Normal circadian sleep rhythm. Sleep urge is greatest at night with a small increase at mid day. Sleep need increases throughout the waking hours and is replenished during sleep.

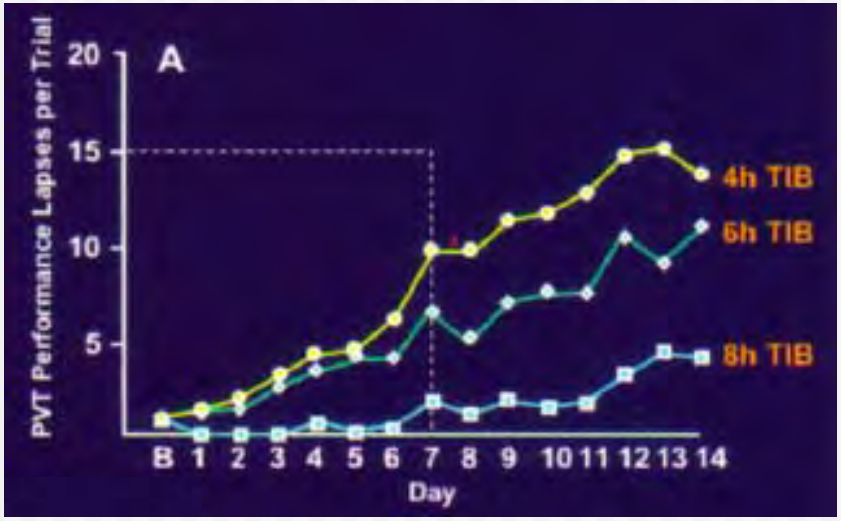
Borbley Hum Neurobiol (1982) - adapted

Sleep deprivation leads to cumulative performance degradation that varies by time of day

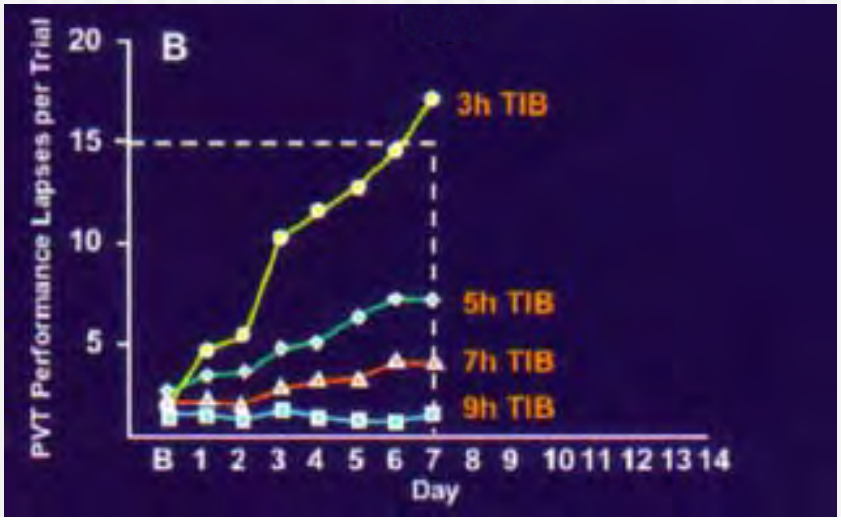


Doran, Dinges, Van Dongen; Sleep 2001

Effects of sleep restriction cumulate over time

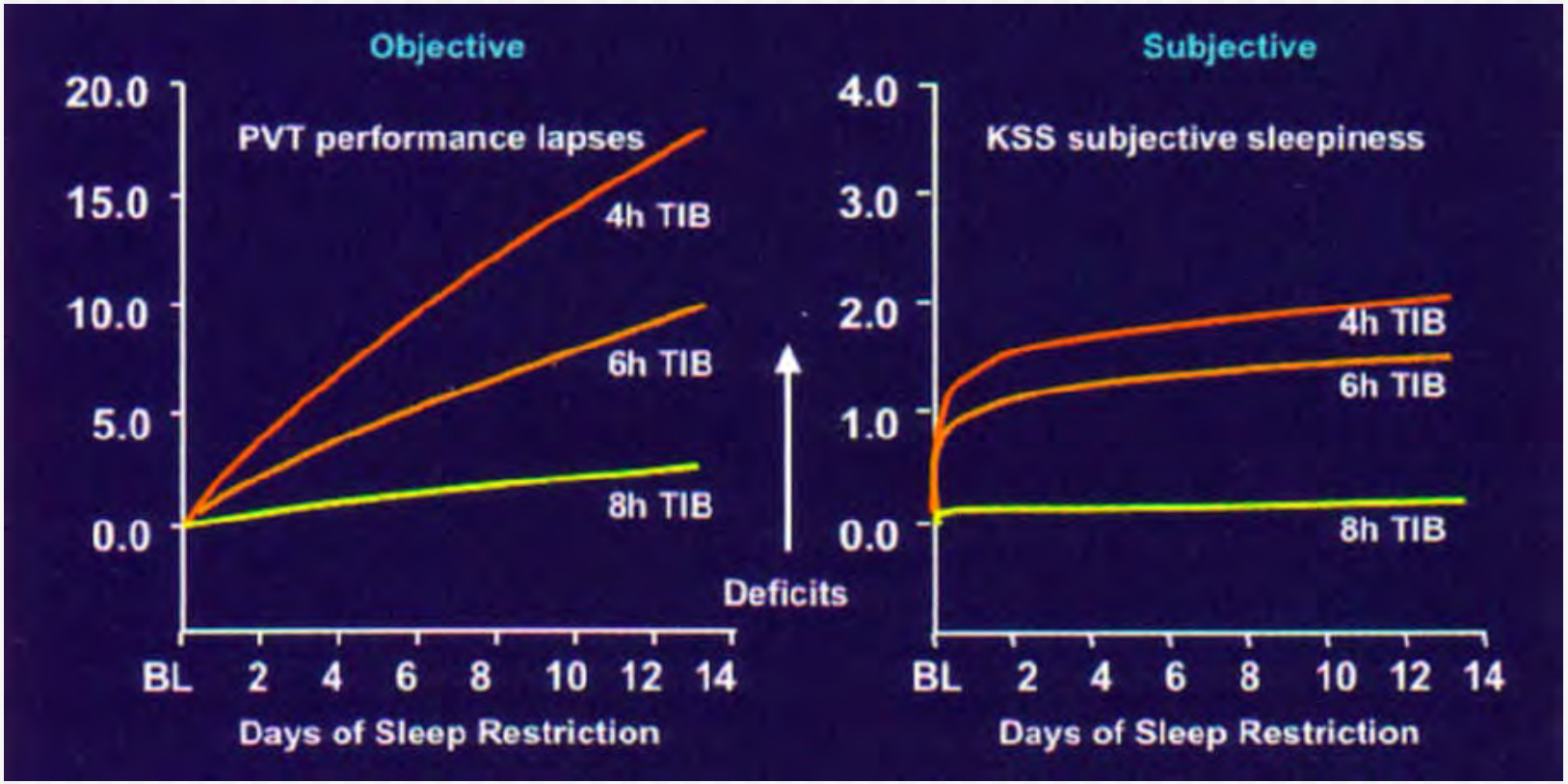


Van Dongen, Sleep (2003)



Belenky J Sleep Res. (2003)

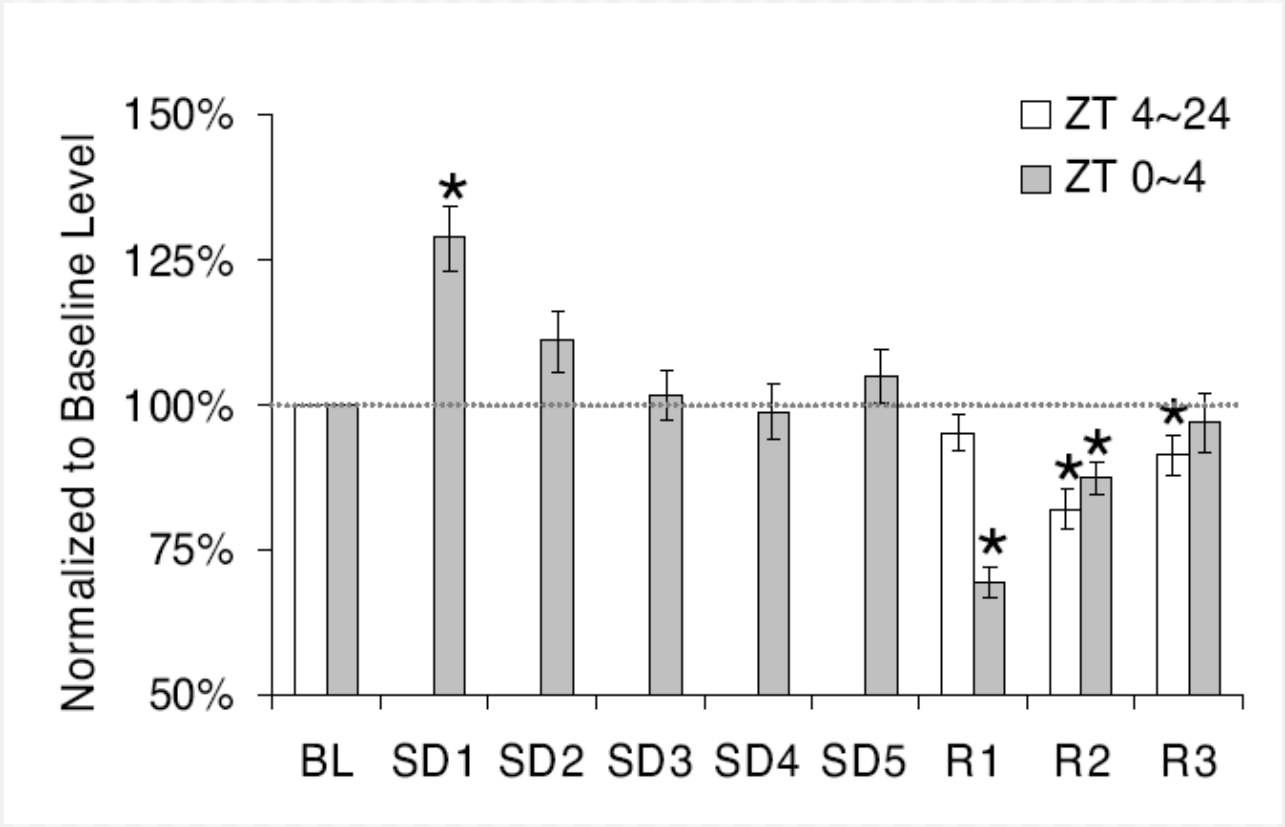
Protracted sleep restriction leads to loss of insight as to its effects



Van Dongen HP, Sleep (2003)

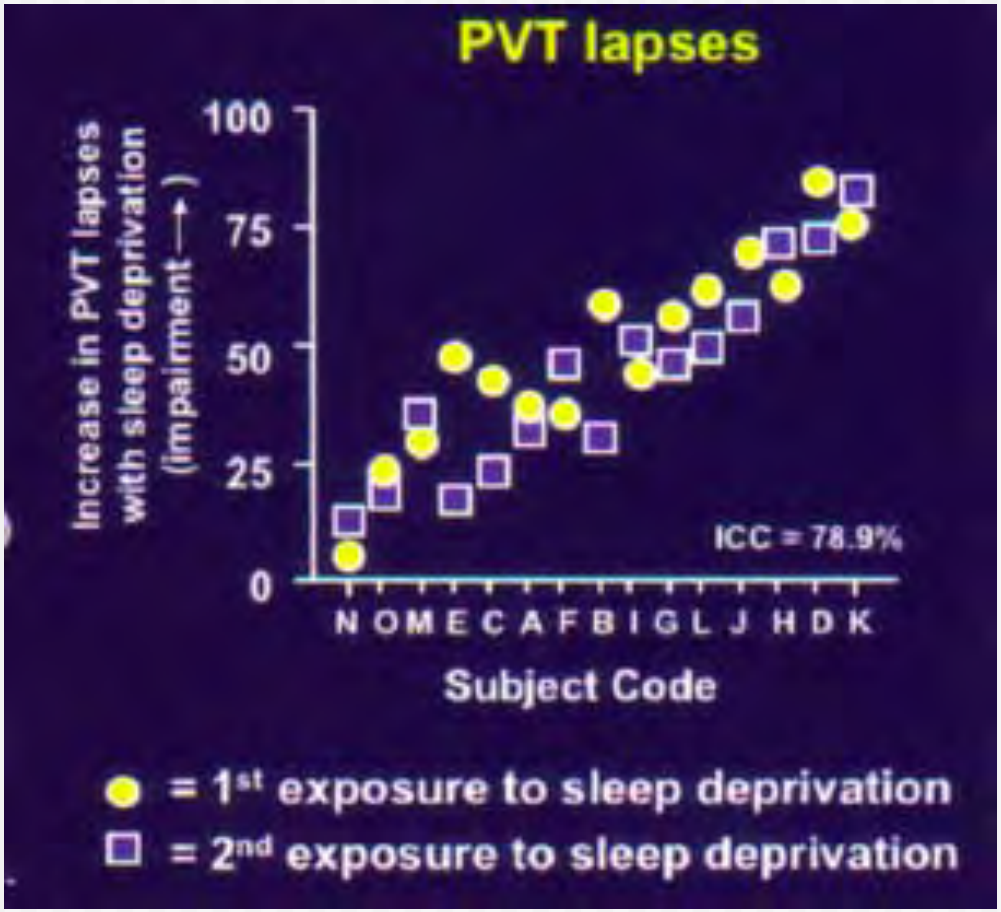
Repeated sleep restriction in rats leads to homeostatic and allostatic responses during recovery sleep

Youngsoo Kim, Aaron D. Laposky, Bernard M. Bergmann, and Fred W. Turek*



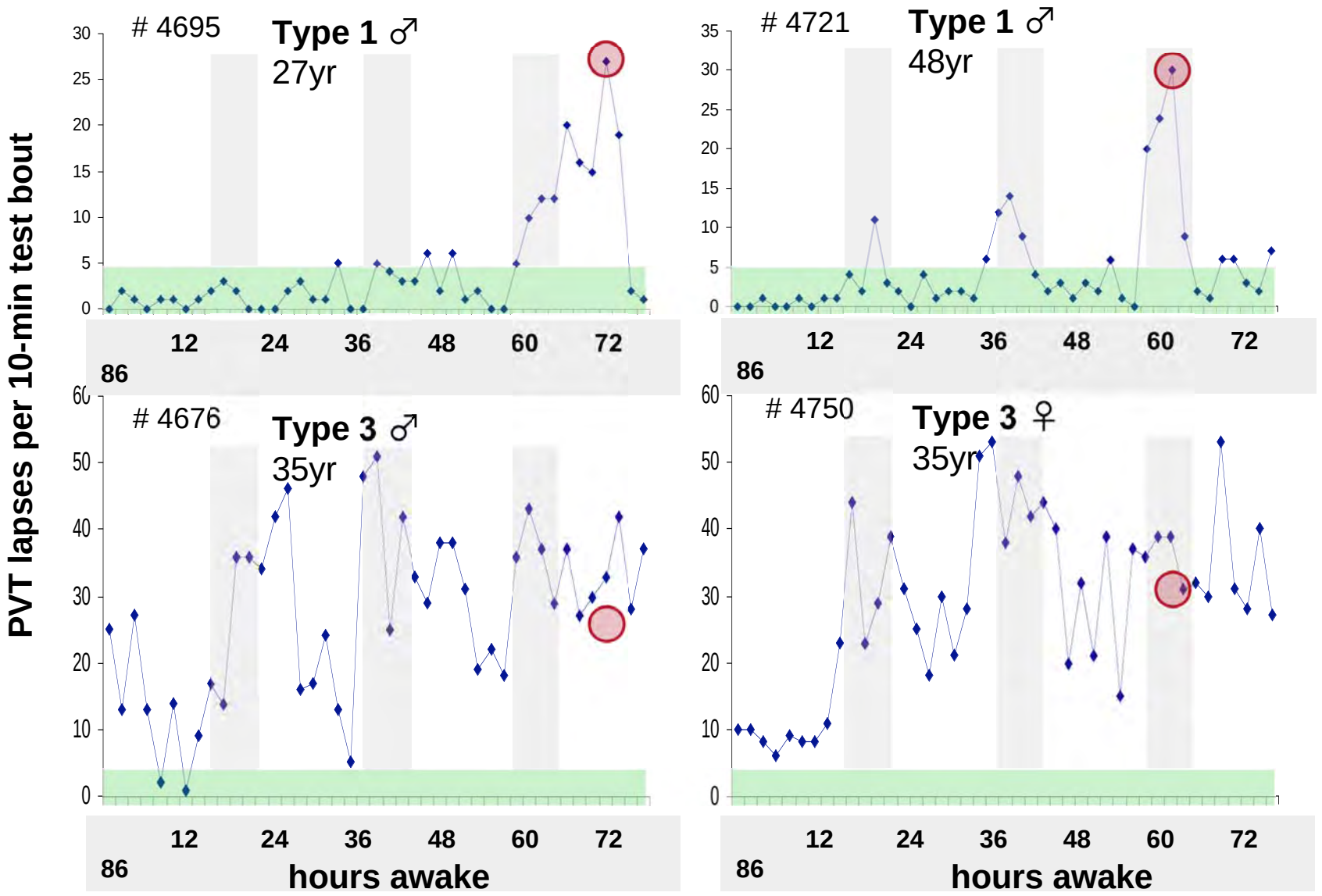
PNAS (2007)

Vulnerability to sleep deprivation shows trait like qualities that differ across individuals



Van Dongen, Sleep (2004)

Type 1 vs. Type 3 responses to total sleep deprivation of 88h



Courtesy of Dinges DF

Consequences of Rapid Transition to Sleep

Sleepy drivers who kill face jail

Sleepy drivers should rest, not carry on

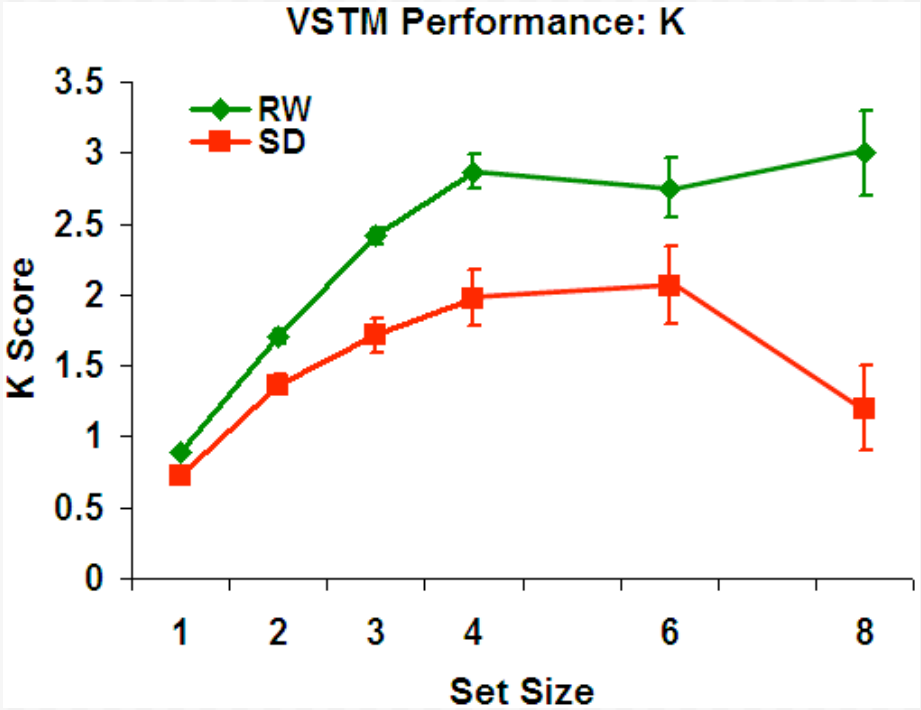
Drivers who kill someone because they have fallen asleep at the wheel are likely to spend at least two years in jail, under new guidelines.

What happens to cognitive and psychomotor performance following sleep deprivation

- Involuntary microsleeps occur
- Attention is unstable: errors of omission and commission
- Response times slow
- ***Short term recall declines***
- Decline in divergent thinking
- Difficulty with response suppression
- Increased response preservation on ineffective solutions

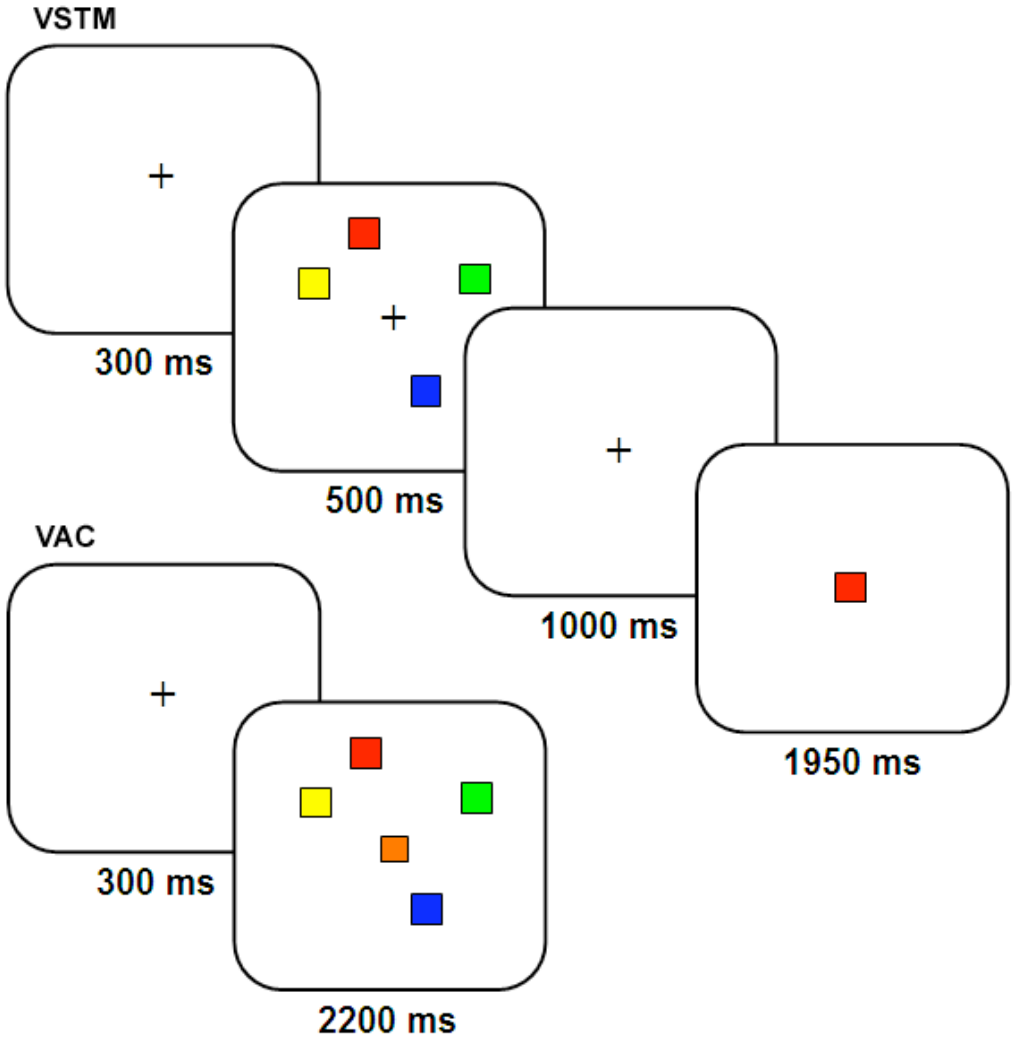
Durmer and Dinges Seminars in Neurology 2005 (adapted)

Visual Short Term Memory capacity drops with sleep deprivation



Chee and Chuah: PNAS(2007)

Testing Visual Short Term Memory



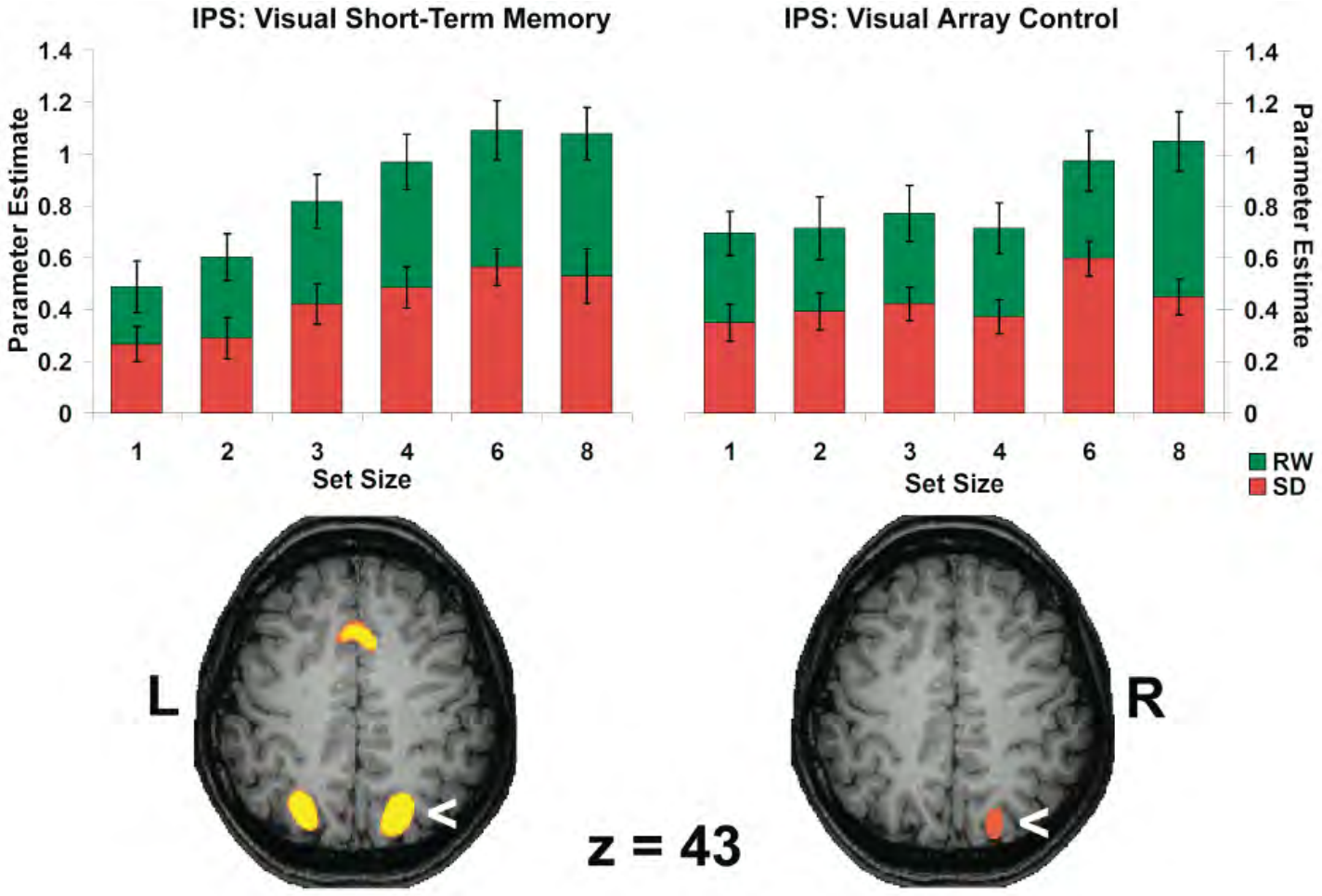
Was this color seen in the array?

Press if a square appears the centre of the display

Chee and Chuah: PNAS(2007)

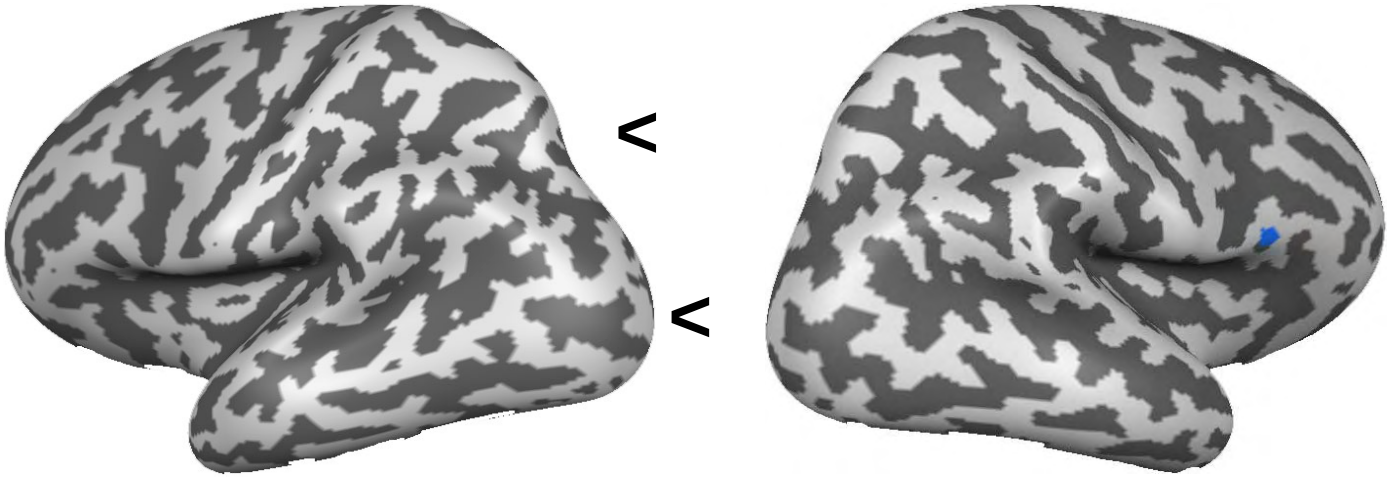
Sleep deprivation reduces parietal activation well *below the capacity limit* of VSTM

ANOVA:
Regions
Showing
Set size effect

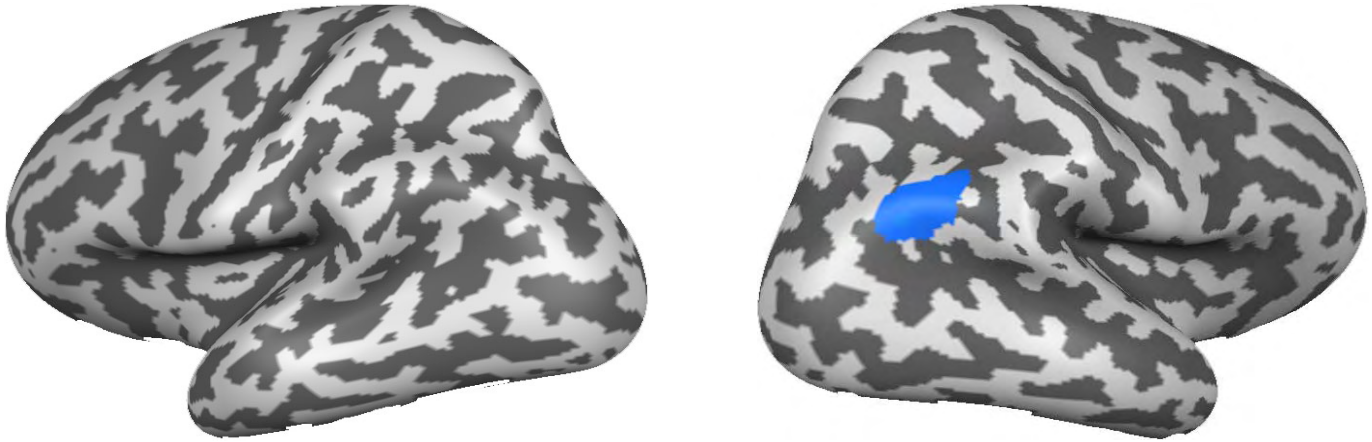


Chee and Chuah: PNAS(2007)

RW



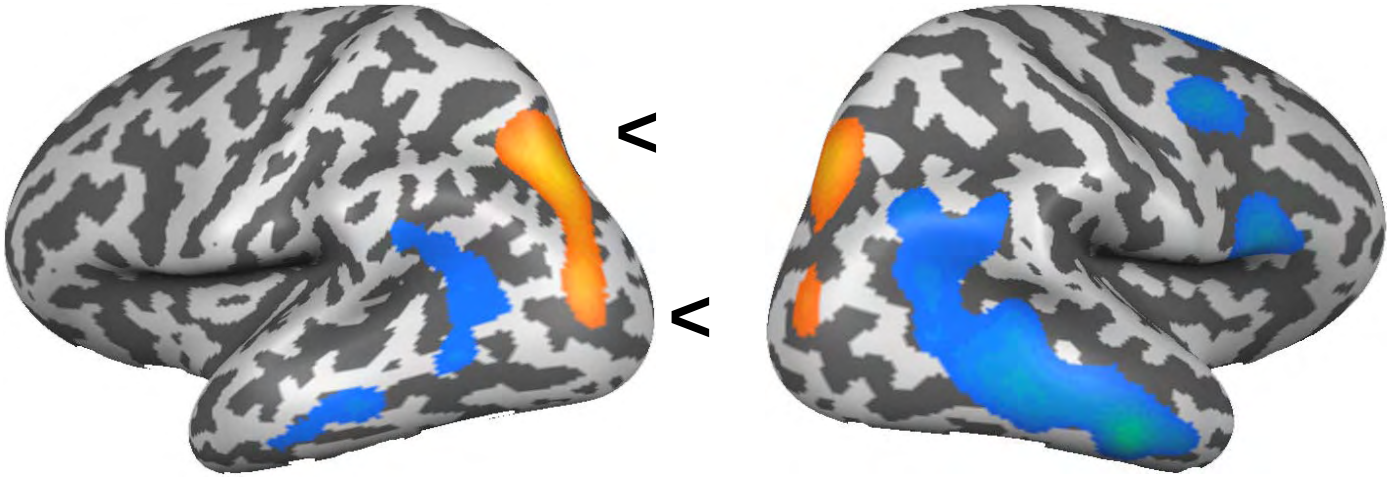
SD



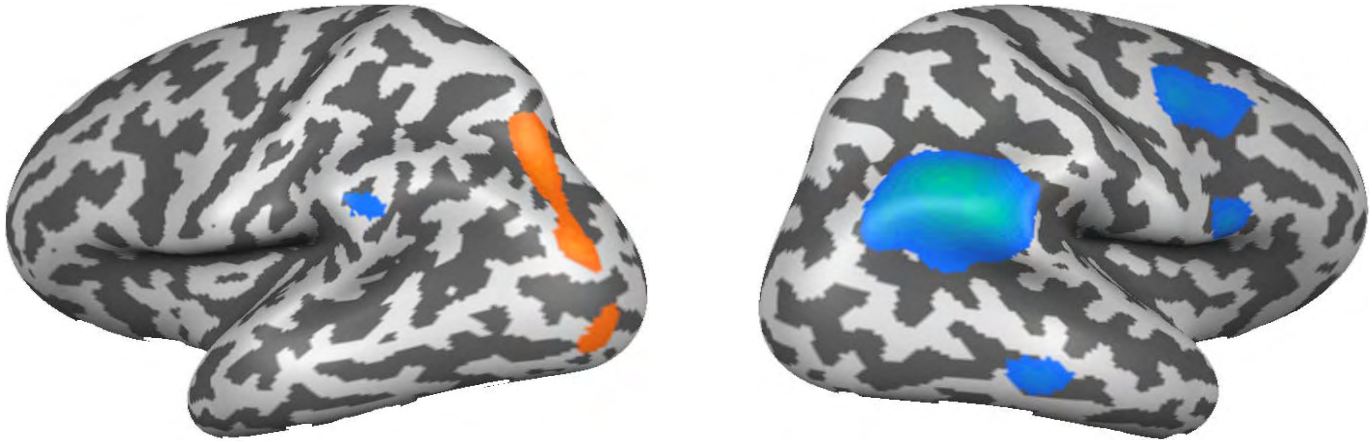
SS2

Memory Load

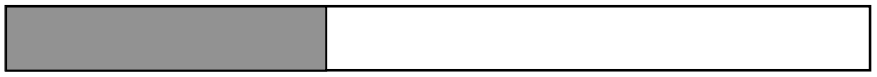
RW



SD

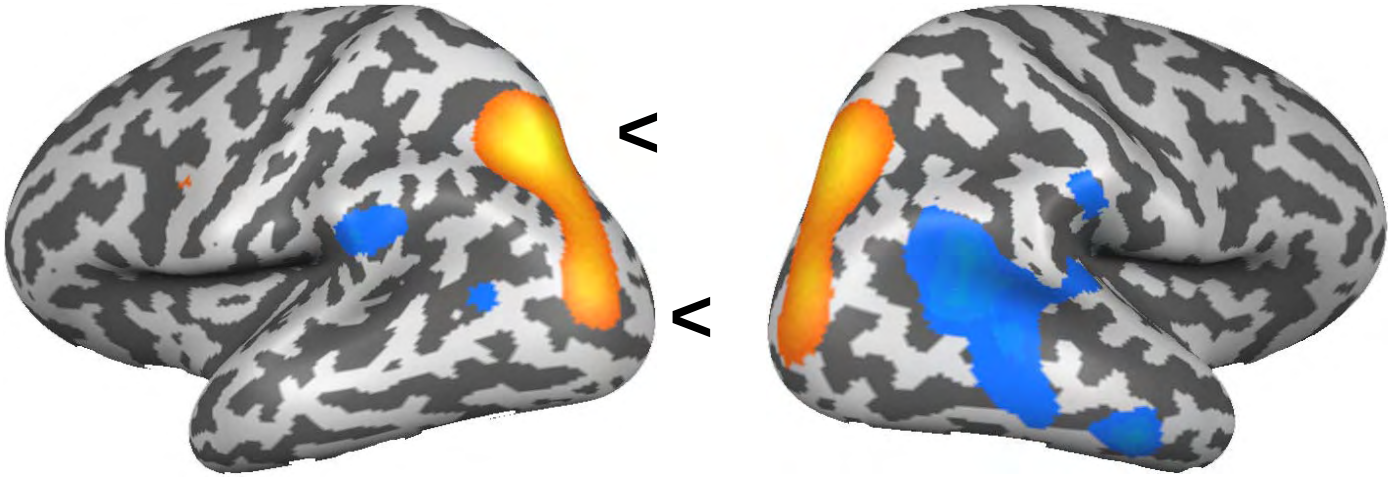


SS3

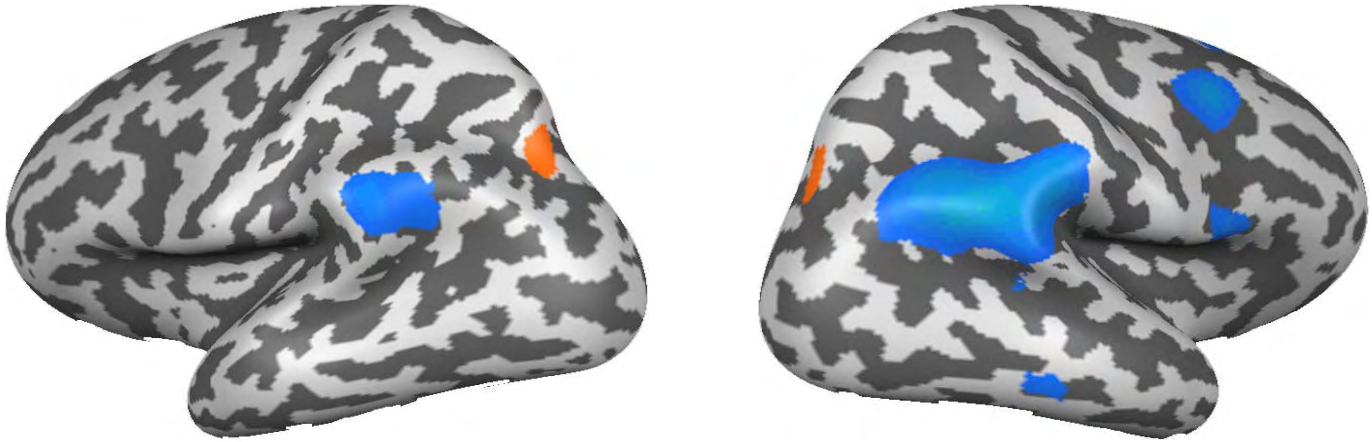


Memory Load

RW



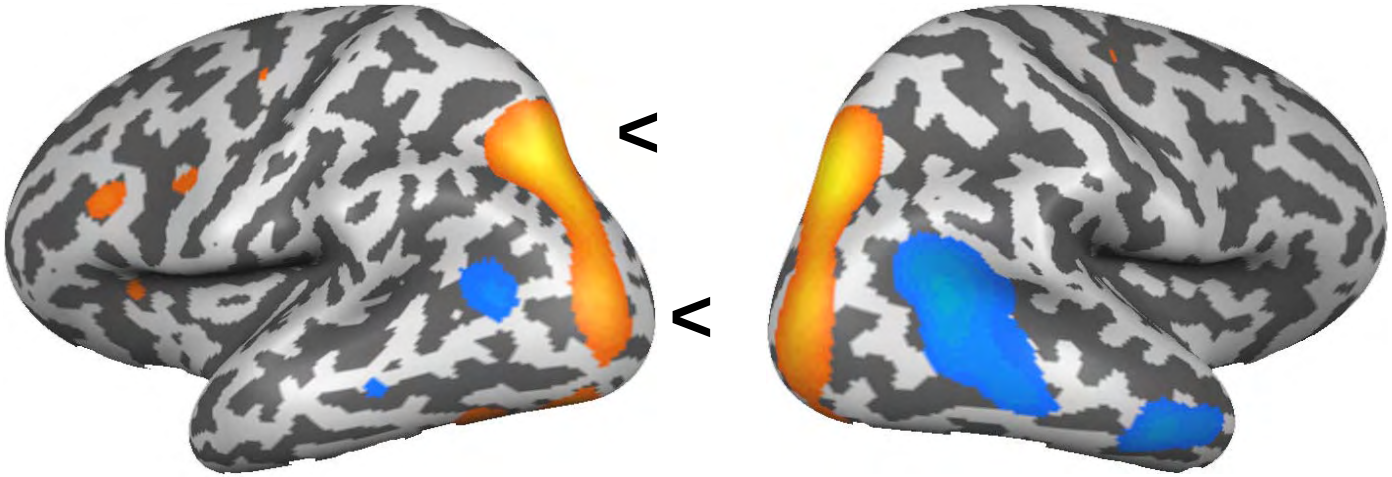
SD



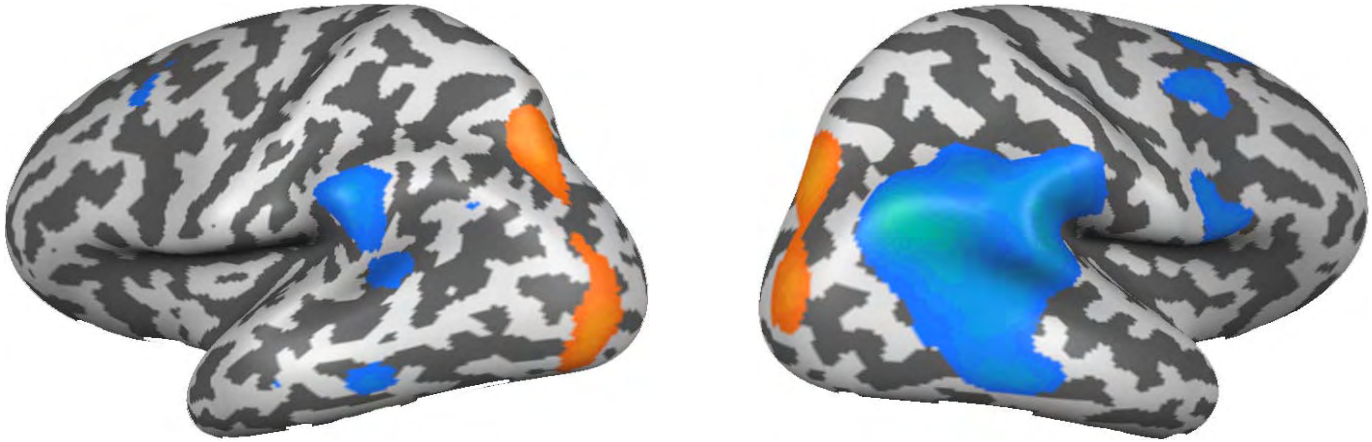
SS4

Memory Load

RW



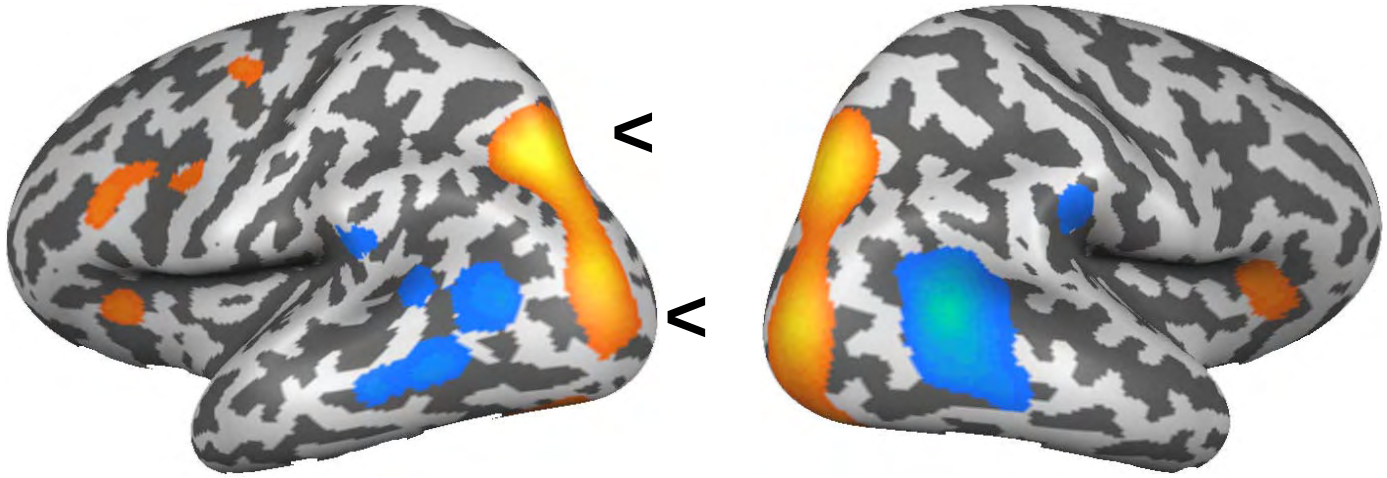
SD



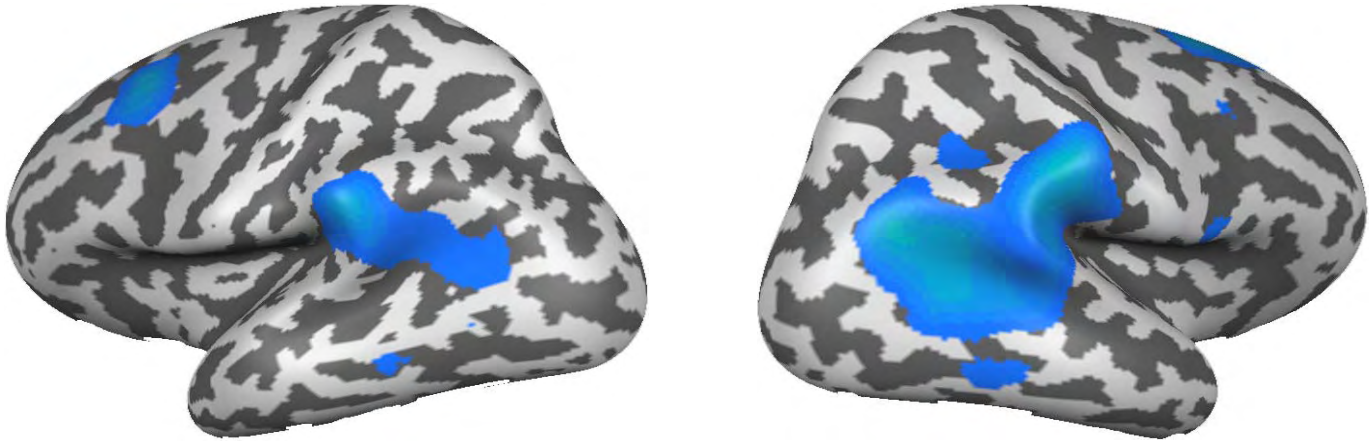
SS6

Memory Load

RW



SD

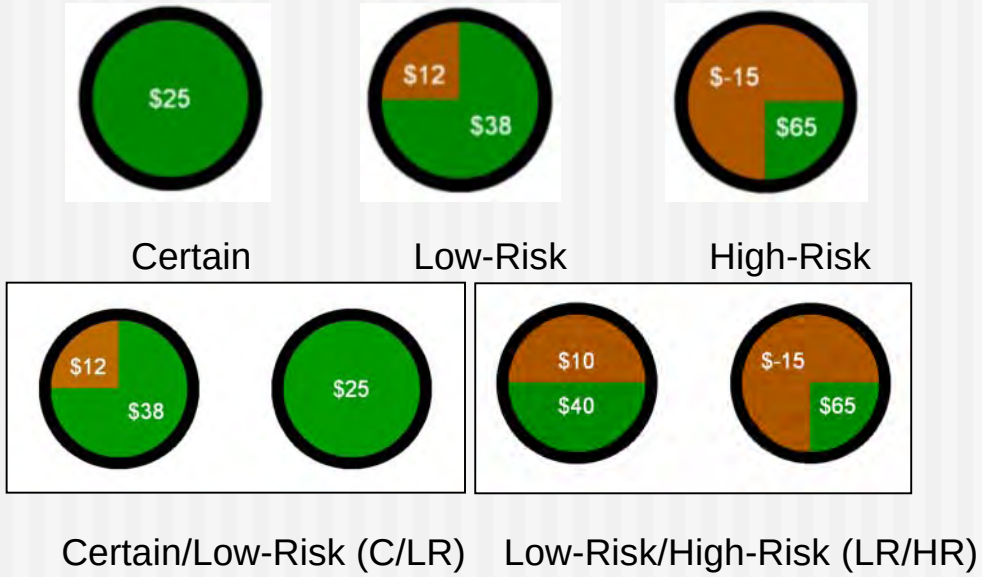


SS8

Memory Load

The Gambling Task

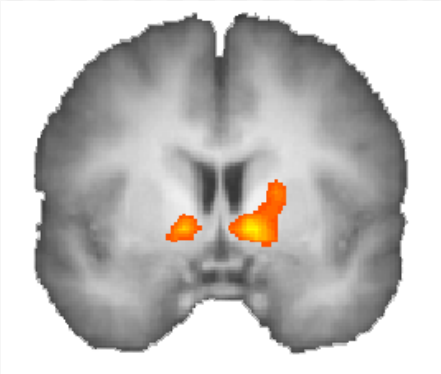
- Choose between two gambles that differ on levels of uncertainty and payout
- Subjects' objective: **Maximize** winnings



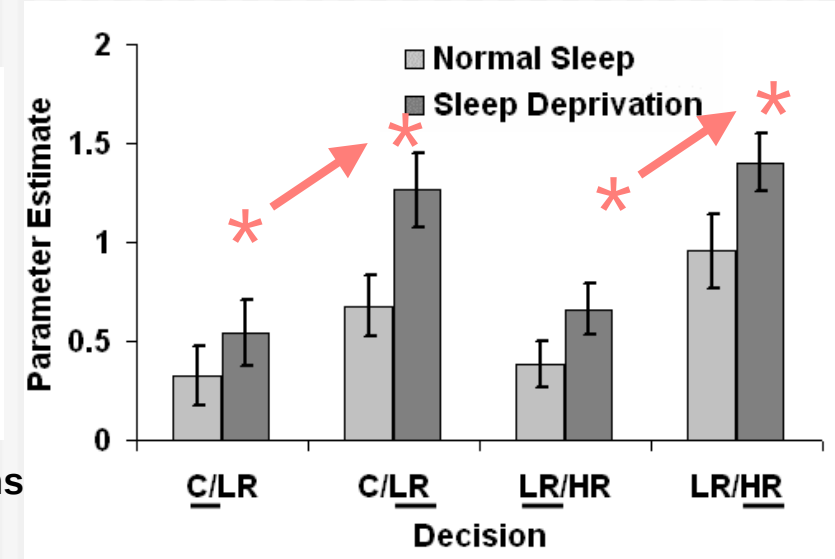
Venkatraman, Chuah, Chee; Sleep (2007)

SD affected a key brain region involved in reward anticipation

Effect of reward anticipation



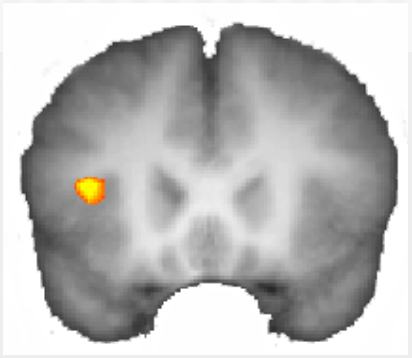
Right Nucleus Accumbens



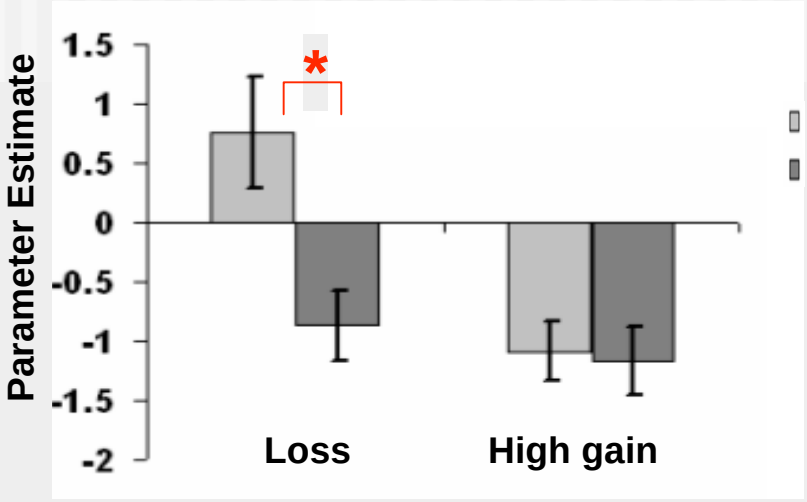
Venkatraman, Chuah, Chee; Sleep (2007)

SD also affects areas involved in responding to loss and disappointment

Representation of a cavalier attitude towards losses following sleep deprivation

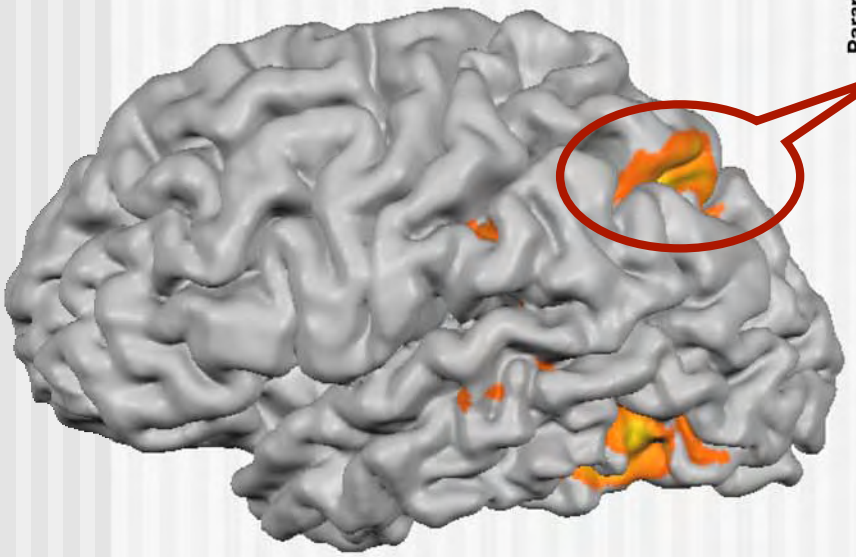


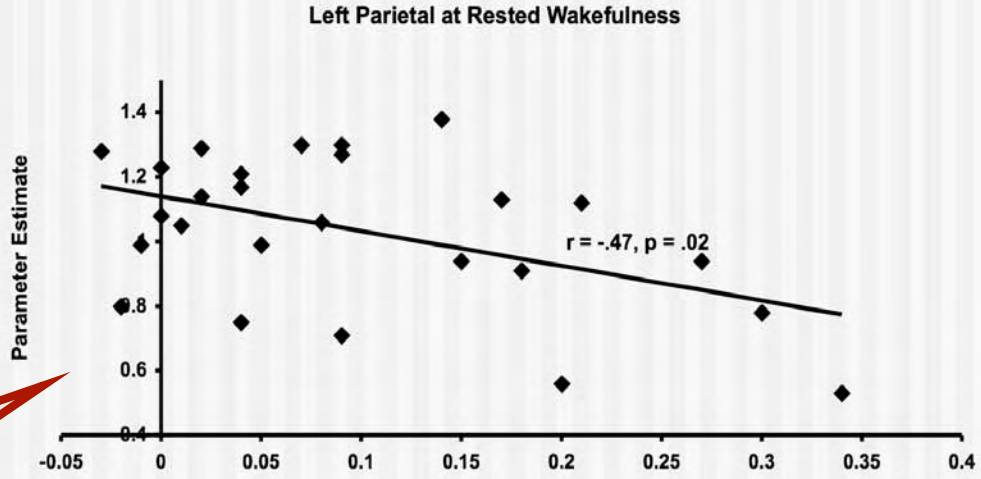
Left Anterior Insula



Venkatraman, Chuah, Chee; Sleep (2007)

In the near future, fMRI may help predict SD resilience

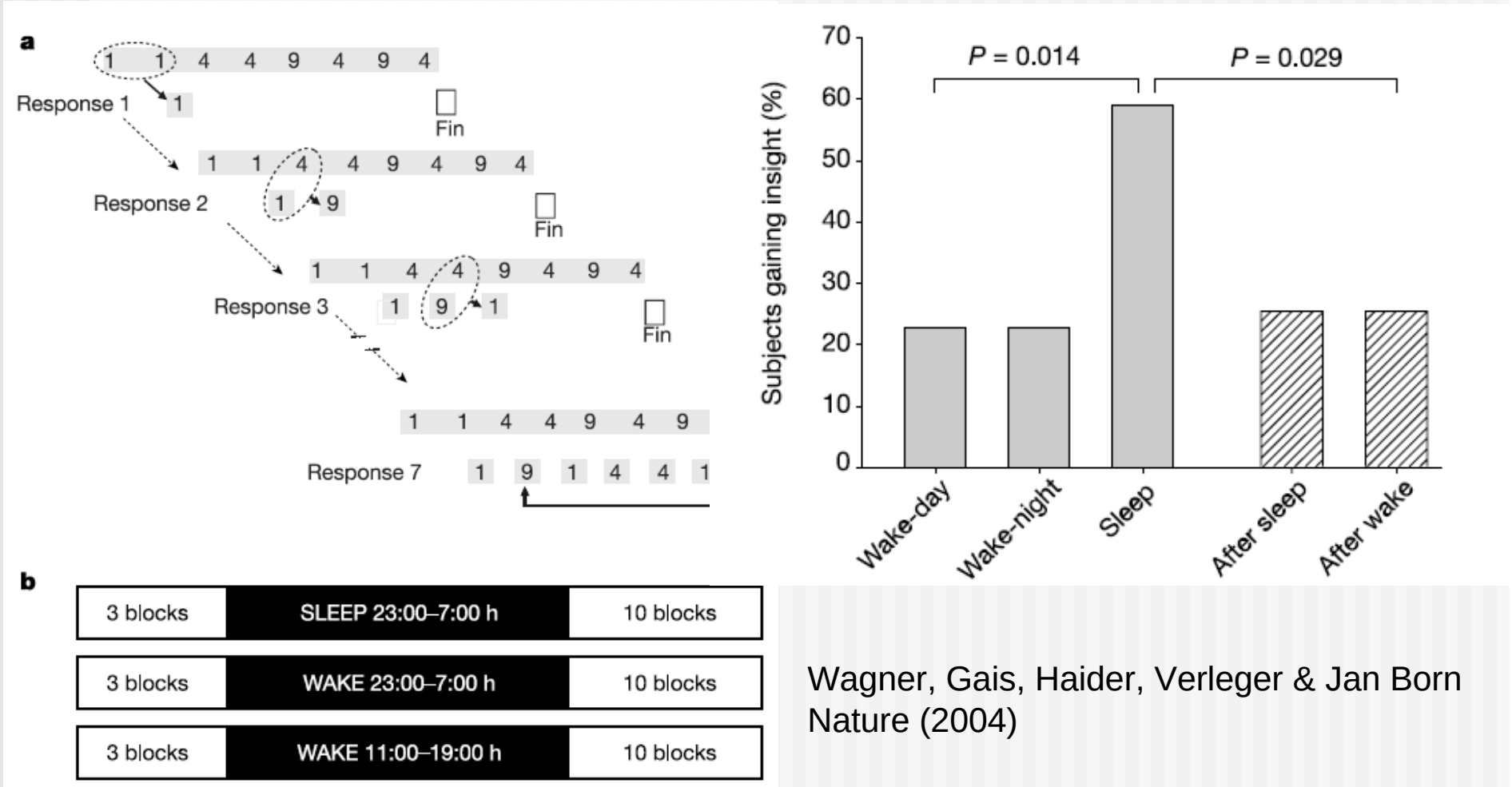




Reduced parietal activation after normal Sleep rest inversely correlates with SD24 performance decline

Chee, Neuroimage (2006)

Sleep unlocks insight into daytime experiences



Wagner, Gais, Haider, Verleger & Jan Born
Nature (2004)

Some serious non-medical consequences of sleep deprivation

- Increased errors on the job[1]
- Reduced activity and productivity[2]
- Increased risk of motor vehicle accidents[3]
- Psychosocial dysfunction[4]

1.Landigran NEJM (2004) 2. Dinges, Sleep Med (2003)
3. Barger NEJM (2005) 4.Dinges, J Sleep Res (1995)

Effect of sleep duration on mortality - complex relationship

- Mortality and sleep duration have a U shaped relationship
- Higher mortality occurs with > 8 hrs of and <4.5 hrs of reported sleep
- Those who report > 8 hrs of sleep
  - Have higher sleep fragmentation
  - Lower sleep efficiency
  - Higher sleep inertia

Kripke DF Am J Psychiatr (2002) Tamakoshi A; Sleep (2004)

Cardiovascular changes in sleep

- Fall in epinephrine
- Fall in heart rate
- Fall in blood pressure (“morning dip”)
- Fall in cortisol (until 5 a.m.)
- HRV (LF / HF) falls
  - sympathetic activity declines
- Overall arrhythmogenicity falls

Veerman; Hypertension (1995)

Cardiovascular responses are altered in sleep disordered breathing

Normal blood pressure (and heart rate response) to sleep is to decline 10% (10-20 mmHg)

- Those who don't are "non-dippers"
- Non-dipping carries risk of
  - Ventricular arrhythmias
  - Cardiac hypertrophy
  - Sudden cardiac death (in women)

Meier-Ewert et al; J Am Coll Cardio (2004) 43:678-83

Blood pressure elevation occurs following sleep deprivation even in healthy persons

Table 1. Heart Rate and Blood Pressure During Total Sleep Deprivation

Baseline	BL (n = 8)	Dep 1 (n = 8)	Dep 2 (n = 7)	Dep 3 (n = 8)	Recovery 1 (n = 7)	Significance
Heart rate (beats/min)	63.0 ± 3.5	65.1 ± 3.7	70.1 ± 3.3	70.9 ± 2.8	69.7 ± 2.9	$F(4,7) = 3.3$, $p < 0.10$
Systolic BP (mm Hg)	121.1 ± 3.8	122.5 ± 2.7	125.4 ± 6.4	128.9 ± 3.0	130.0 ± 4.2	$F(4,7) = 313.3$, $p < 0.0001$
Diastolic BP (mm Hg)	68.1 ± 2.9	70.0 ± 2.4	72.0 ± 4.0	72.9 ± 2.8	71.4 ± 3.6	$F(4,7) = 3.4$, $p < 0.10$

Data are presented as the mean value ± SEM.
BL = baseline; BP = blood pressure; Dep = deprivation (day).

Table 2. Heart Rate and Blood Pressure During Partial Sleep Deprivation

Baseline	BL	Dep 10	Condition by Day Interaction	BL vs. Day 10
HR in sleep (beats/min)	75.0 ± 4.1	79.5 ± 7.3	$F(1,7) = 5.89$, $p < 0.05$	NS
HR in PSD (beats/min)	75.2 ± 2.6	97.0 ± 4.8		$t(7) = 4.59$, $p < 0.01$
SBP in sleep (mm Hg)	127.8 ± 6.2	137.3 ± 3.5	NS	
SBP in PSD (mm Hg)	113.6 ± 6.7	135.2 ± 9.4		
DBP in sleep (mm Hg)	73.5 ± 7.4	86 ± 2.9	NS	
DBP in PSD (mm Hg)	68.6 ± 3.0	85.4 ± 4.8		

Data are presented as the mean value ± SEM.

Meier-Ewert et al; J Am Coll Cardio (2004) 43:678-83

Endocrine changes

- Hypothalamic pituitary axis:
  - Altered temporal profile of GH output
  - Reduced TSH output
  - Increased CRF release
- Increased sympathetic drive
- Elevated evening levels of cortisol
- Decreased glucose tolerance

Spiegel K; Lancet (1999)

Appetitive control goes awry

- **Leptin** levels decrease following SD
  - Produced by fat cells
  - Signals satiety to the brain
  - Signal decrease notable at night
- **Ghrelin** levels increase
  - Peptide secreted by the stomach
  - Increases appetite; esp for high carb. foods

Spiegel K, J Clin Endocrinol Metab (2004), Taheri S, Sleep (2004)

Endocrine changes can be sustained

- Changes following short term total sleep deprivation are reversible but
- Chronic sleep restriction is harmful
  - Elevated evening cortisol may promote insulin resistance --> obesity and diabetes

Cauter, Knutson, Leprout, Spiegel 2004

Risk of metabolic syndrome is increased with sleep deprivation

- Confluence of negative effects on blood pressure, glucose tolerance, cortisol, appetitive control and pro-inflammatory cytokines

Resnick; Diabetes Care (2003) editorial: Zee & Turek Arch Int. Med (2006)

Countermeasures

- Napping and schedule adjustment
- Caffeine
  - Most pervasive performance enhancer
- Amphetamines
  - Used in a military setting for years
  - Increased risk of risk taking behavior
  - Rebound fatigue and depression
- Tiagabine : selective SWS enhancer
- Modafanil
  - Decreases sleepiness and maintains cognitive performance in shift-workers with minimal effect on daytime sleep[1]
- CX 717 - Ampakine [2]

Czeisler C: NEJM (2005), Porrino PLOS Biology (2005)

Long distance driving, coffee and napping

Table. Line Crossings per Participant and Driving Session

Participant	Order of Sessions	Line Crossings, *n*			
		Daytime Condition	Coffee Condition	Placebo Condition	Nap Condition
1	Daytime, nap, coffee, placebo	0	1	11	6
2	Daytime, nap, placebo, coffee	1	3	2	1
3	Daytime, nap, coffee, placebo	0	0	3	3
4	Daytime, nap, placebo, coffee	1	0	13	6
5	Daytime, coffee, placebo, nap	0	1	2	1
6	Daytime, coffee, placebo, nap	0	0	2	0
7	Daytime, coffee, nap, placebo	0	13	17	8
8	Daytime, coffee, nap, placebo	0	2	0	0
9	Daytime, placebo, nap, coffee	0	0	11	0
10	Daytime, placebo, coffee, nap	0	0	11	0
11	Daytime, placebo, coffee, nap	0	0	1	0
12	Daytime, placebo, nap, coffee	0	0	0	0
Total		2	20	73	25

Philip et al; Ann. Int Med (2006)

Children and the elderly appear to take naps more often than young adults

- Among children, toddlers and young children are most likely to take naps
- The propensity to nap decreases with age and by the teens, few persons nap
- About 8% of young adults nap
- Napping increases again in the elderly (~25%)
  - Weakening of the amplitude of the circadian drive
  - Reduction in nocturnal sleep duration
- **Naps tend to occur in the afternoon (14:00-16:00)**

Weissbluth: Sleep (1995); Buysse DJ: J Am Geriatr Soc (1992)

Benefits of napping

- After a period of learning, sleep greatly enhances learning[1]
  - Most important with nocturnal sleep
- Naps can benefit intense daytime learning[2]
- Decreases early evening sleepiness[3] (elderly)
- **Boosts performance for the sleep deprived and shift workers**[4]
- Reduces cardiovascular mortality in men[5]
- Enhances safety for long haul drivers

1. Born; The Neuroscientist (2006) 2. Mednick et al: Nat. Neurosci (2002) 3. Monk; Sleep (2001) 4. Smith-Coggins et al; 5.Ann Emerg Med (2006); 6. Naska et al; Arch Int Med (2007)

What is the ideal duration of a nap?

- 10 minutes has been shown to be *optimal
- Shorter: no benefit; appears to be a need for a fixed period of Stage 2 sleep or onset of SWS
- Longer (typically 30 minutes and beyond: problems with sleep inertia
  - Sleep inertia occurs when much SWS occurs

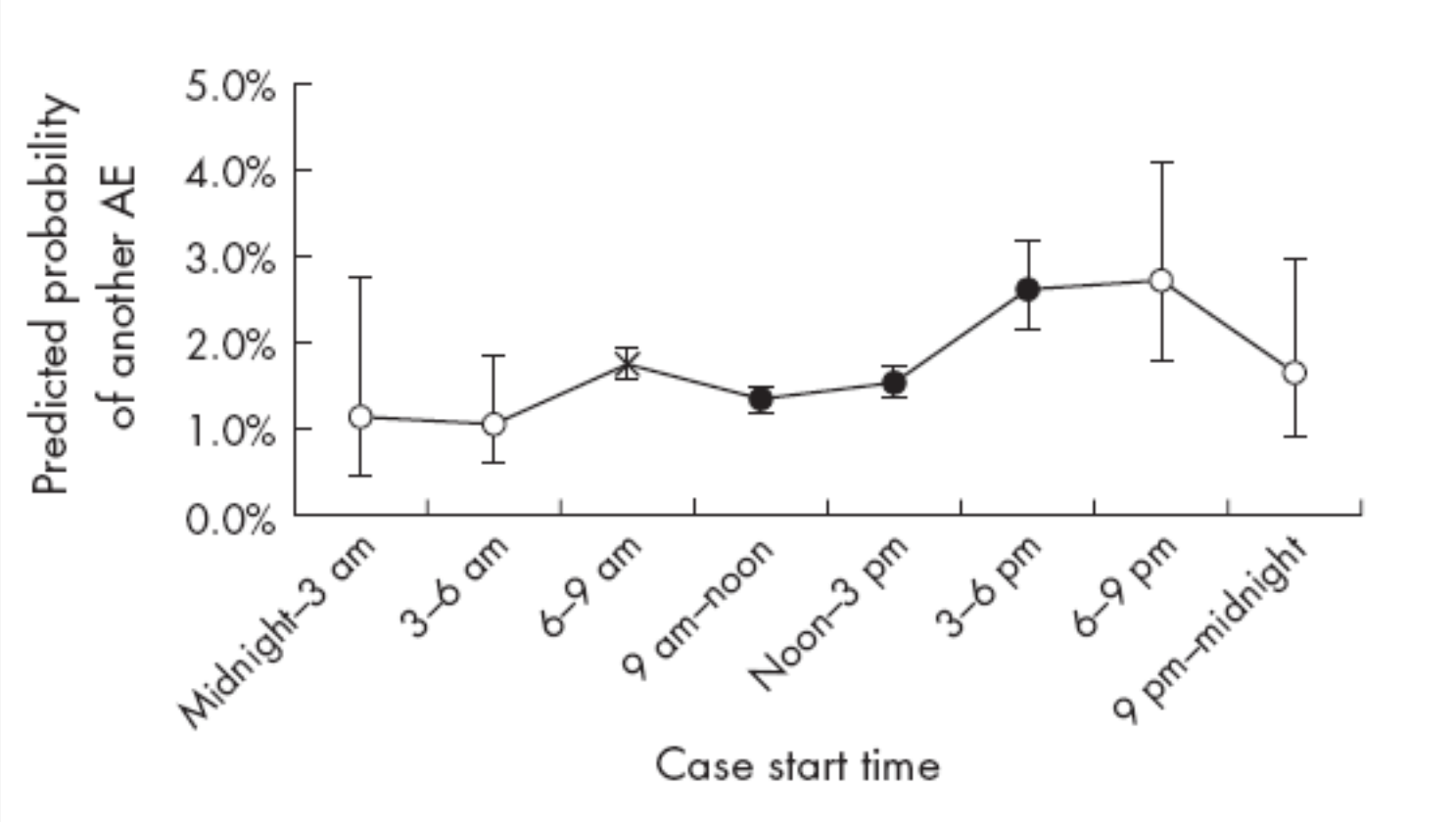
* Brooks and Lack; Sleep (2006)

What is sleep inertia?

- Impaired alertness and performance for approx. 30 minutes after awakening from a nap
- Slows response time but not accuracy of task performance

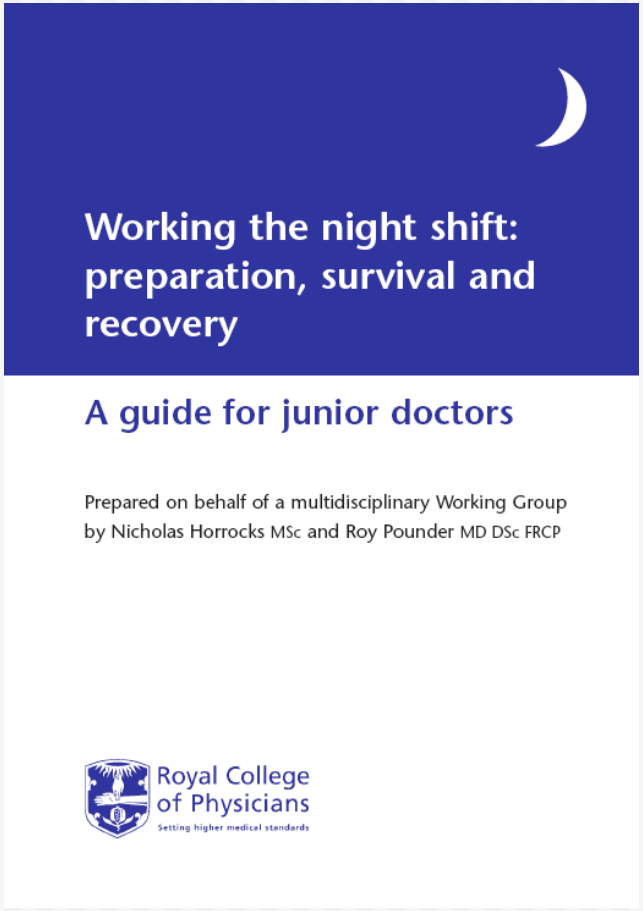
Tassi: Sleep Med Rev (2000)

Time of day affects surgical accidents



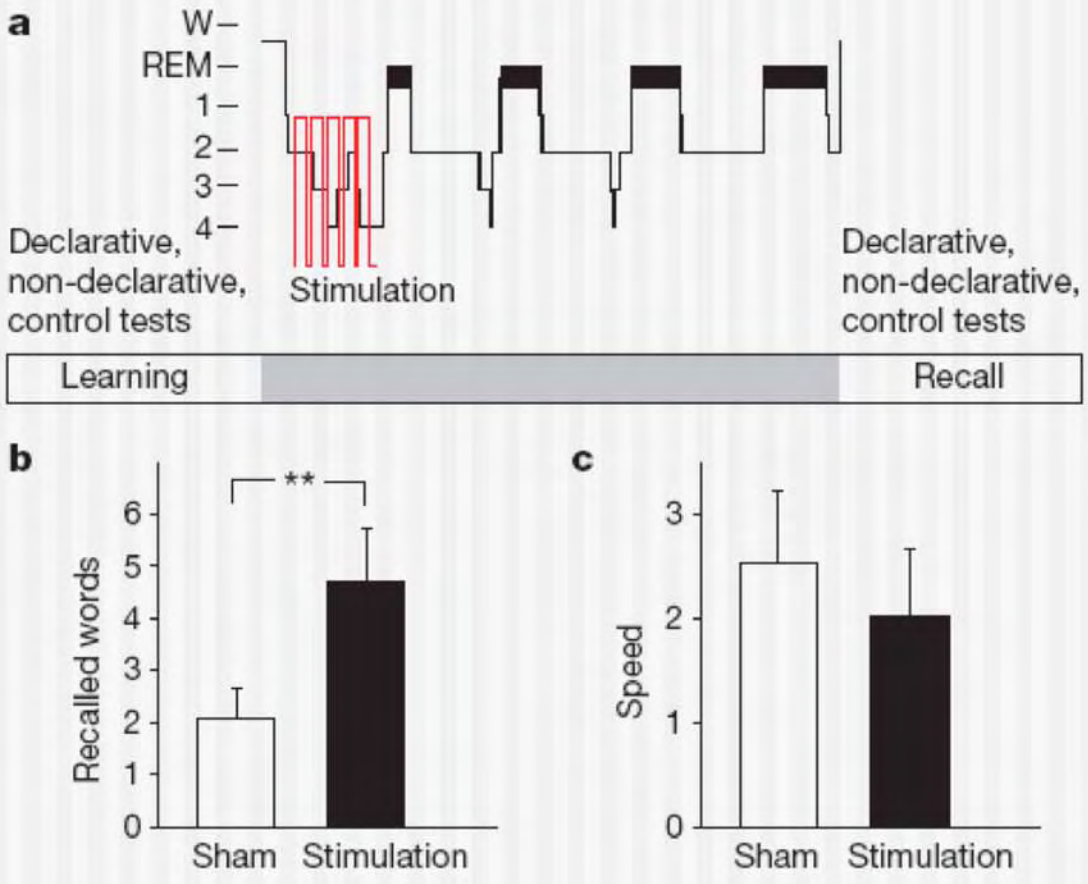
Wright et al: Qual. Saf. Health Care 2006;15;258-263

A good evidence based guide



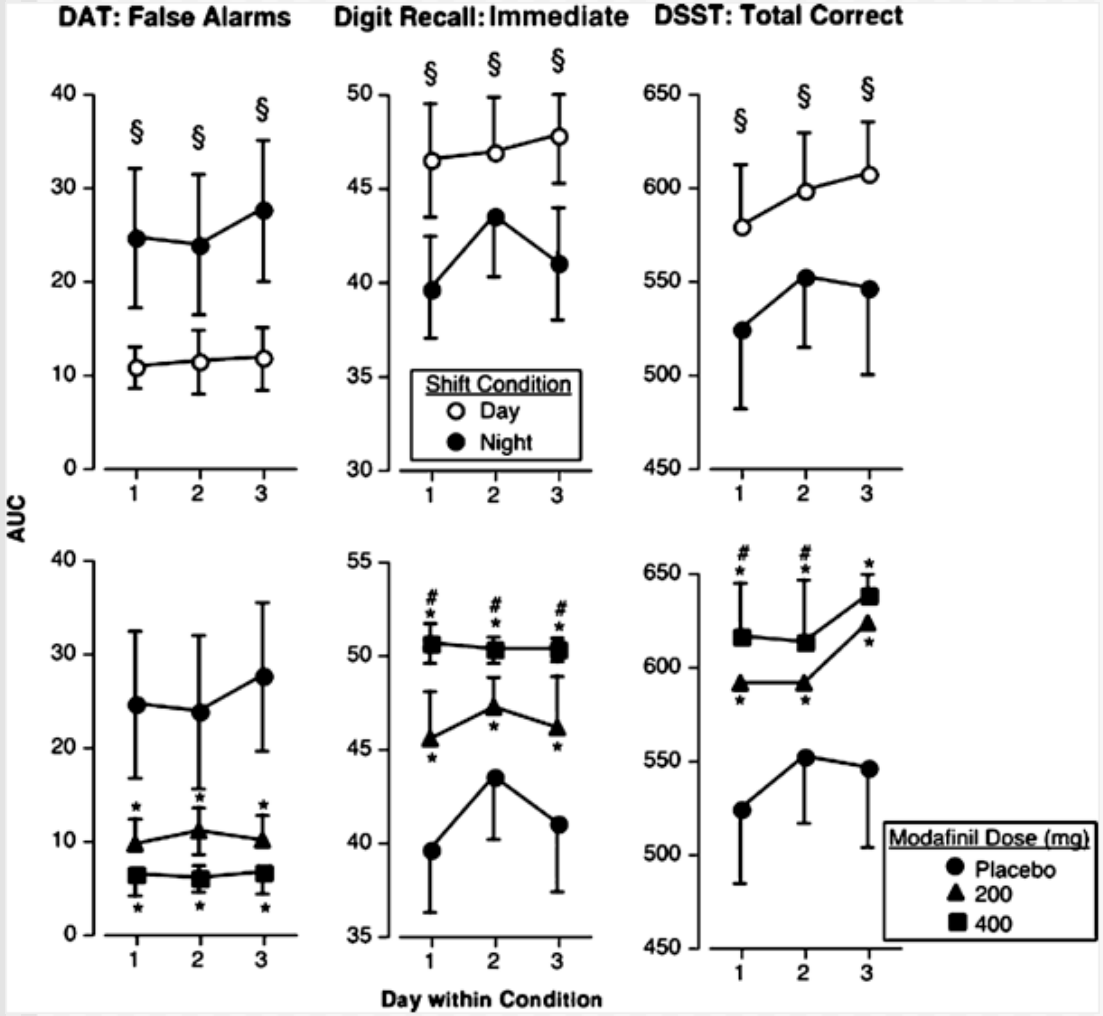
http://www.rcplondon.ac.uk/pubs/books/nightshift/nightshiftbooklet.pdf

Rhythmical electrical stimulation may improve declarative memory



Marshall, Helgadottir, Molle, Born; Nature (2006)

Modafinil improves shift work performance



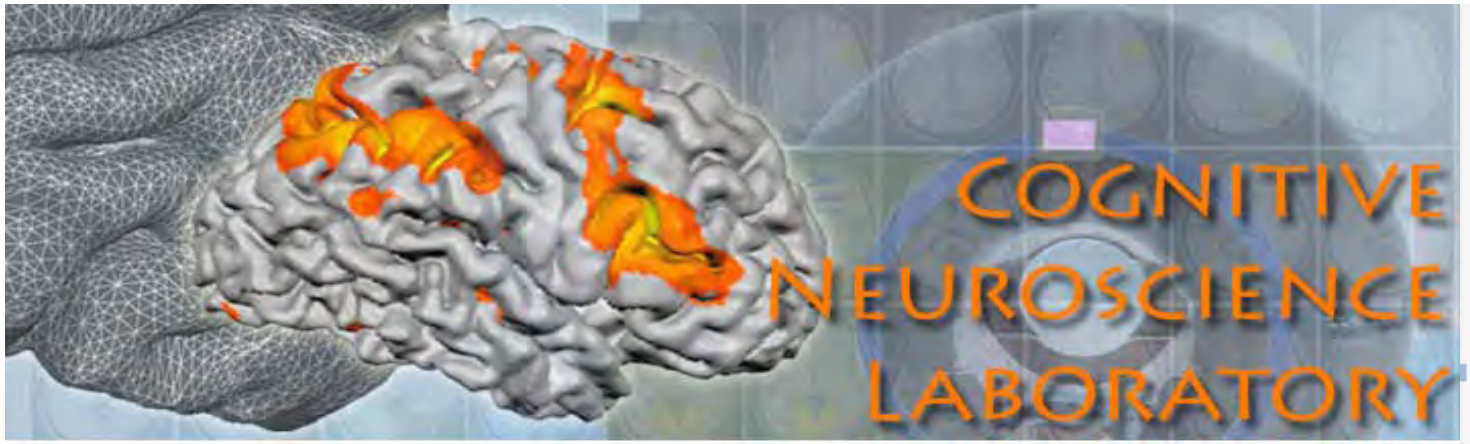
Hart et al; Neuropsychopharmacology (2006)

Countermeasures against sleepiness

- Countermeasures are not without side effects
- Apart from napping, they are best thought of as short term lifestyle options and should not be used as a long term solution

Conclusions

- Sleep has a restorative function and is essential, not optional
- Voluntary sleep restriction has significant negative impacts on health and cognition
- If you can’t get enough sleep at least be aware of when you are at greatest risk to yourself and others
- Napping and coffee are presently the most well established countermeasures



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http://www.cogneuro-lab.org/index.htm