

# Sleep Physiology and Connection to Chronic Disease States



**Presented by Dr. Allison Brager**  
Sleep Physiology Expert

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# About the Presenter

Dr. Allison Brager is an expert in sleep physiology and relevance to issues of mental health. She serves in several leadership and scientific advisory board positions with professional research societies, industry, and professional, Olympic, and collegiate teams.



She has over 30 publications in flagship journals of medicine, neuroscience, and physiology widely featured by large media outlets and is author of the popular science book *Meathead: Unraveling the Athletic Brain*. She has a Sc.B from Brown University and a PhD from Kent State University.

# **Sleep Physiology and Connection to Chronic Disease States**

Dr. Allison Brager  
Army Neuroscientist  
Author of Meathead: Unraveling the Athletic Brain

## **Disclaimer**

The opinions herein are mine and do not represent those of the United States Army, the Department of Defense, or the United States Government

**Why do we spend 1/3 of our lives asleep?**

## Two types of sleep in a 90 min cycle

- **NREM (non rapid eye movement) sleep**
  - deep sleep
  - 85% of total nighttime sleep
- **REM (rapid eye movement) sleep**
  - active brain in a paralyzed body
  - 15% of total nighttime sleep \*\*dreaming

# Functions of sleep

- **Rejuvenate (NREM sleep)**
  - heal up and store energy
    - Growth hormone, testosterone\*\*
- **Learning and Memory (REM sleep)**
  - declarative (facts), episodic (events), procedural (motor)

Hours

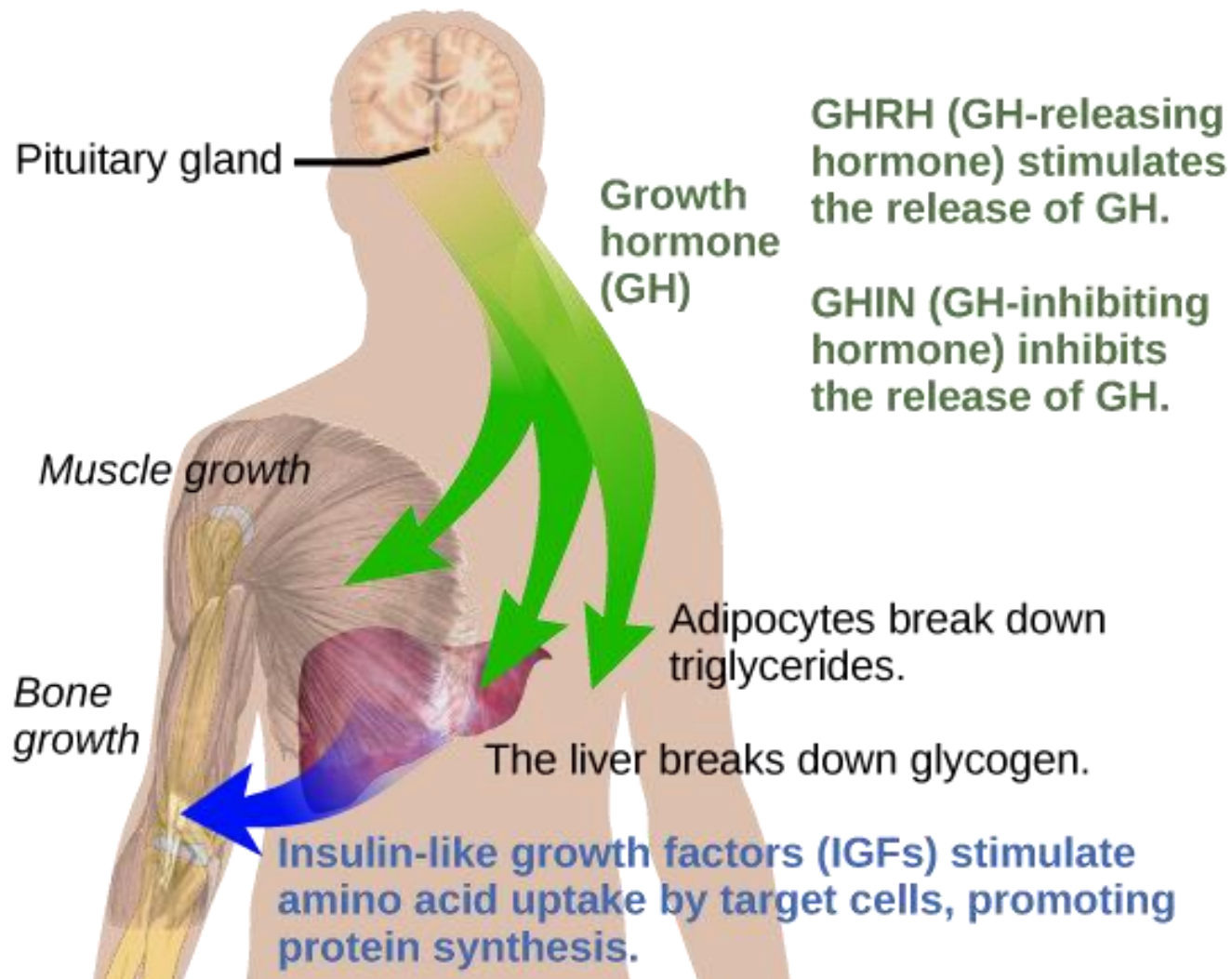
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8

**More NREM, less REM**

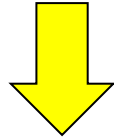
**More REM, less NREM**

# Rejuvenation with NREM sleep

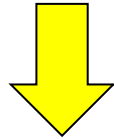




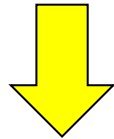
# With sleep deprivation.....



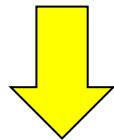
**Reaction time**



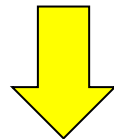
**Coordination**



**Power**

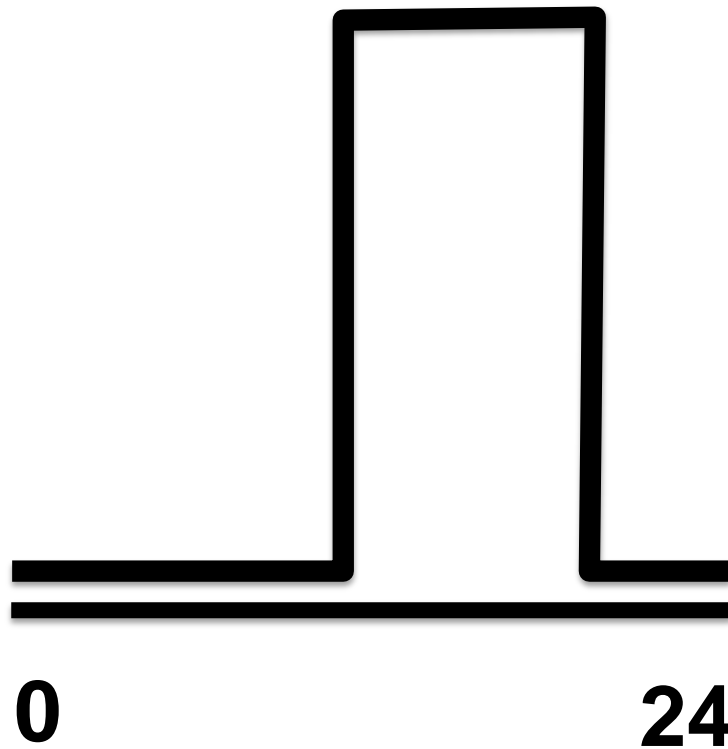


**Agility**

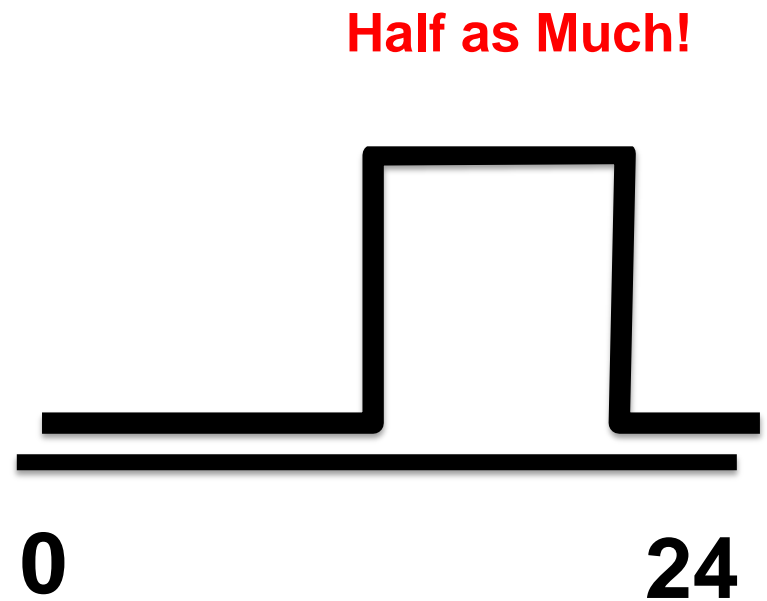


**Teamwork\*\***

# Sleep to Perform (Growth Hormone)

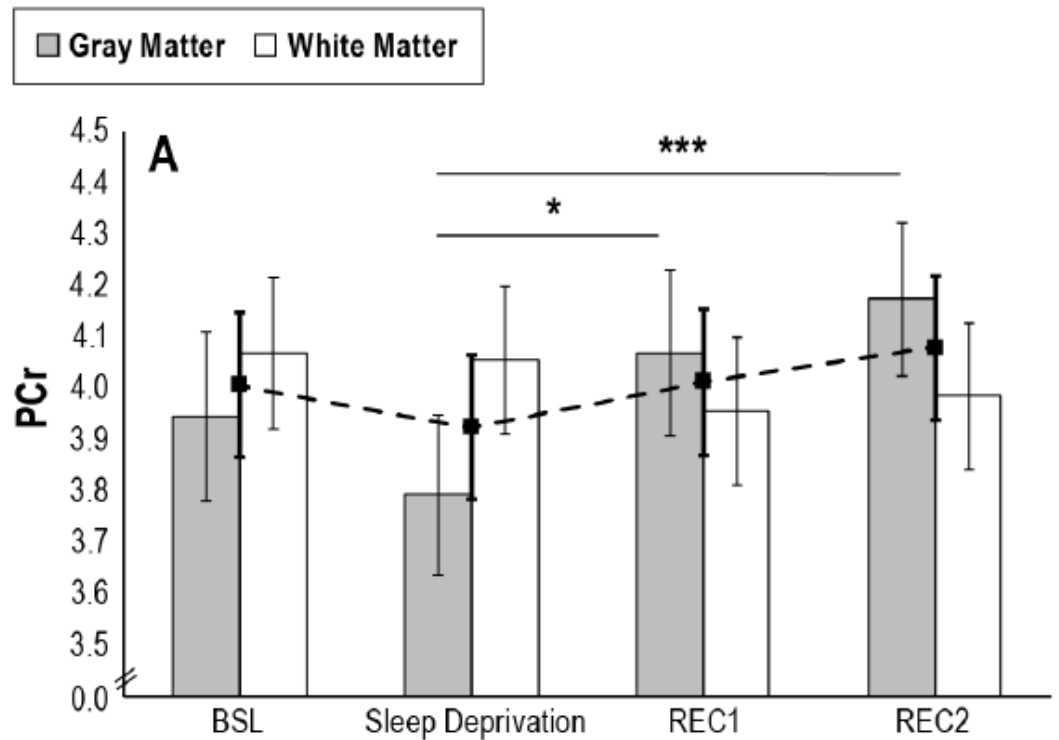
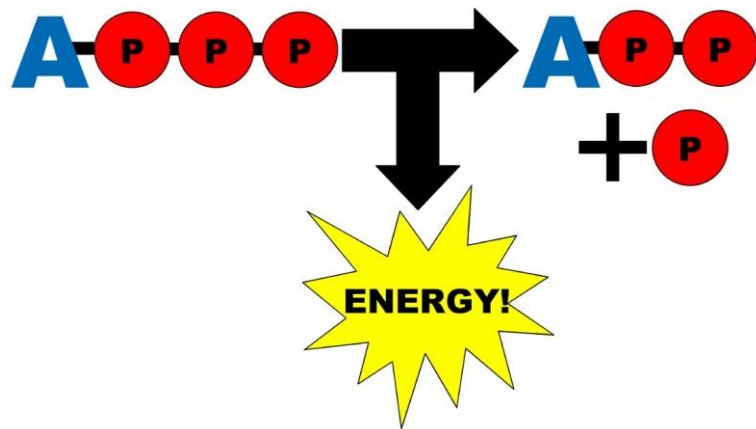


**Sleep 8 hours every night**



**Sleep 4 hours every night**

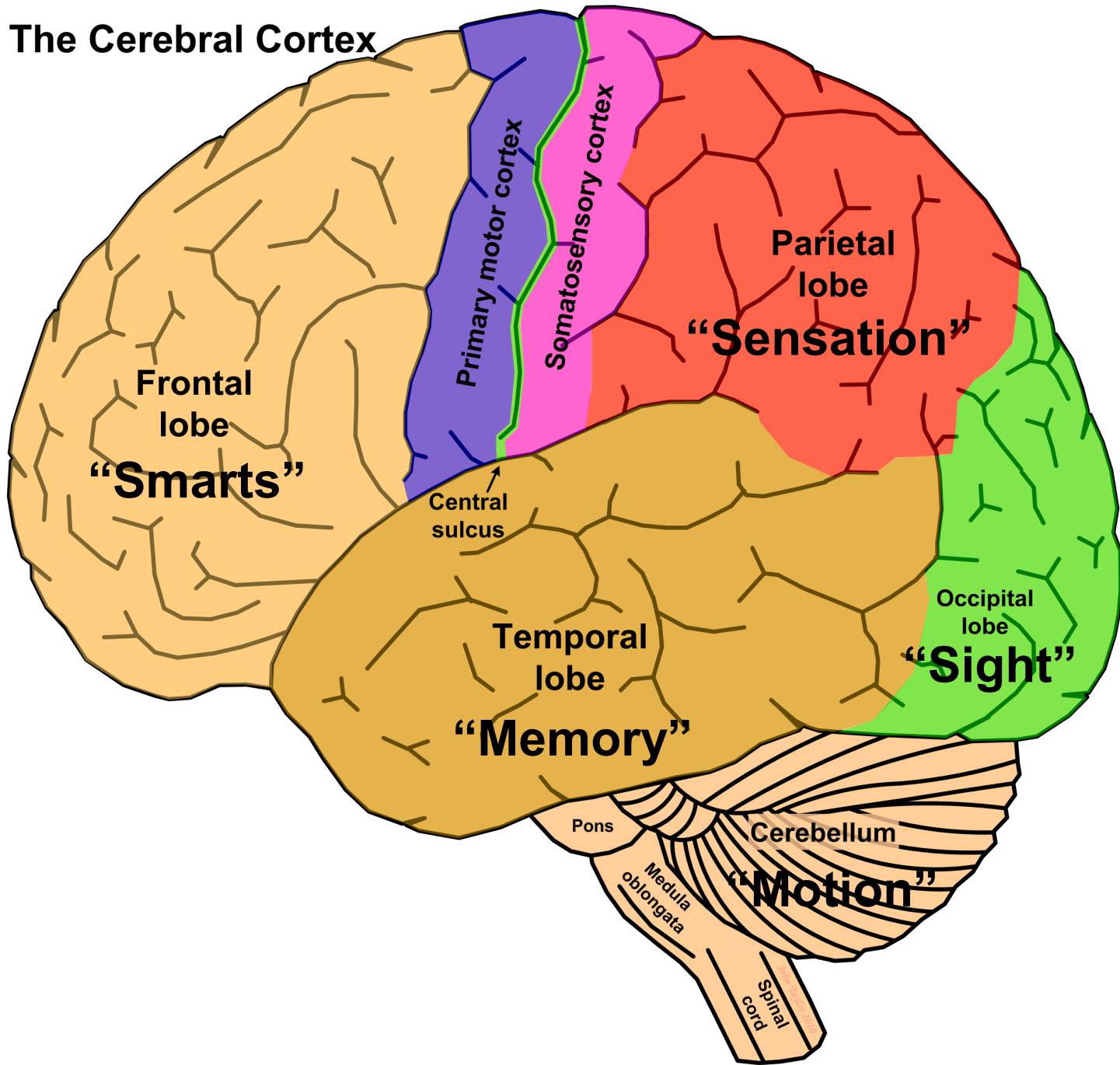
# Sleep to Perform (Cellular Energy)



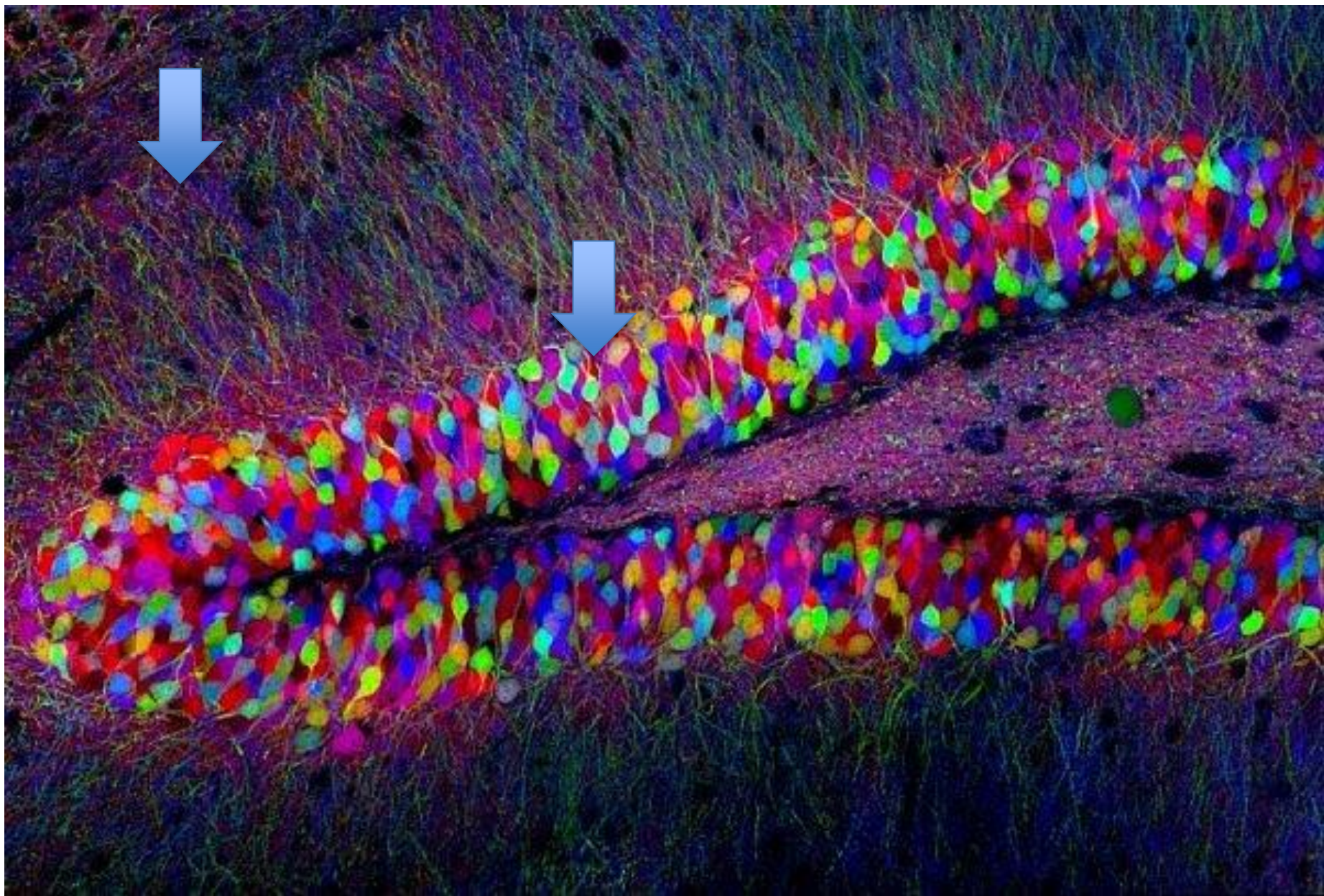
Plante et al. 2014

**How is sleep regulated and how is it related to holistic health?**

# The Cerebral Cortex





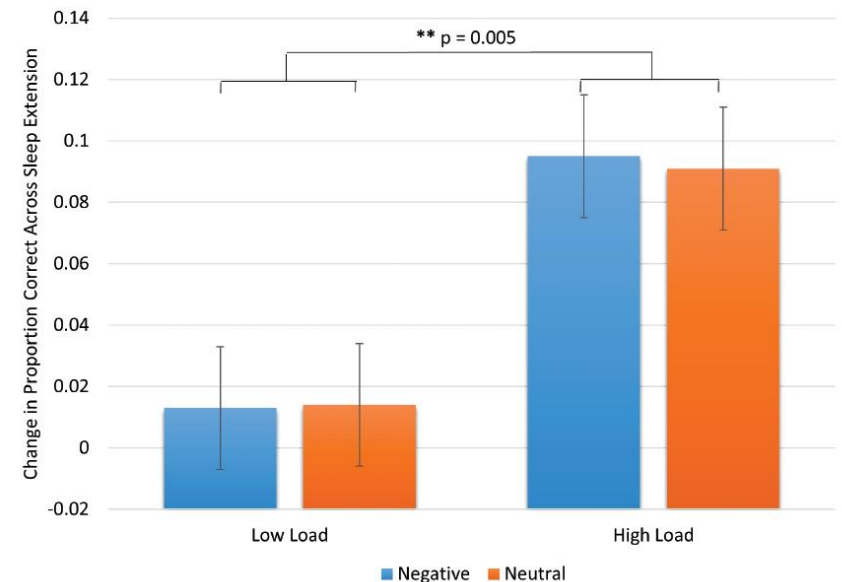
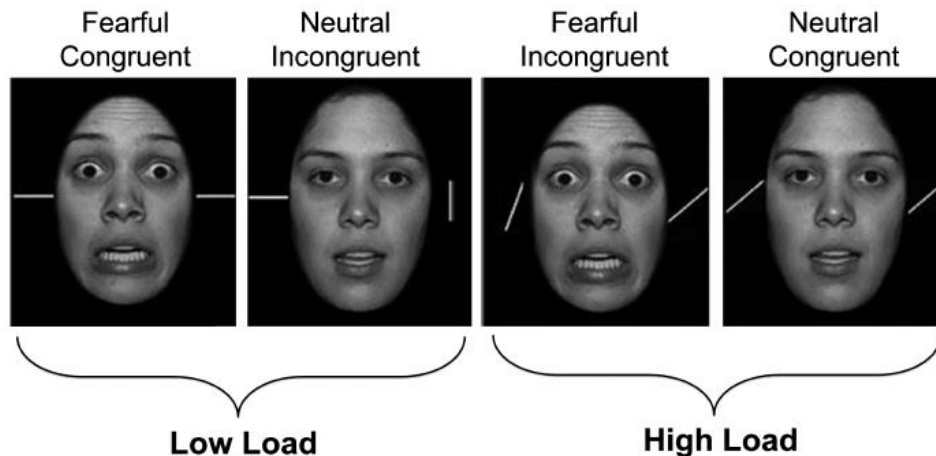


# Effect of cognitive load and emotional valence of distractors on performance during sleep extension and subsequent sleep deprivation

Sara E. Alger<sup>1,\*</sup>, Allison J. Brager<sup>1</sup>, Thomas J. Balkin<sup>1,2</sup>, Vincent F. Capaldi<sup>1</sup> and Guido Simonelli<sup>1</sup>

<sup>1</sup>Behavioral Biology Branch, Walter Reed Army Institute of Research, Silver Spring, MD and <sup>2</sup>Oak Ridge Institute for Science and Education, Oak Ridge, TN

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Email: [sara.e.alger.civ@mail.mil](mailto:sara.e.alger.civ@mail.mil).





# Muscles Hold a Key to Sleep Recovery

A protein in skeletal muscles helps mice recover from sleep deprivation.

Sukanya Charuchandra

Aug 31, 2018



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## EDITOR'S CHOICE IN CELL & MOLECULAR BIOLOGY

### The paper

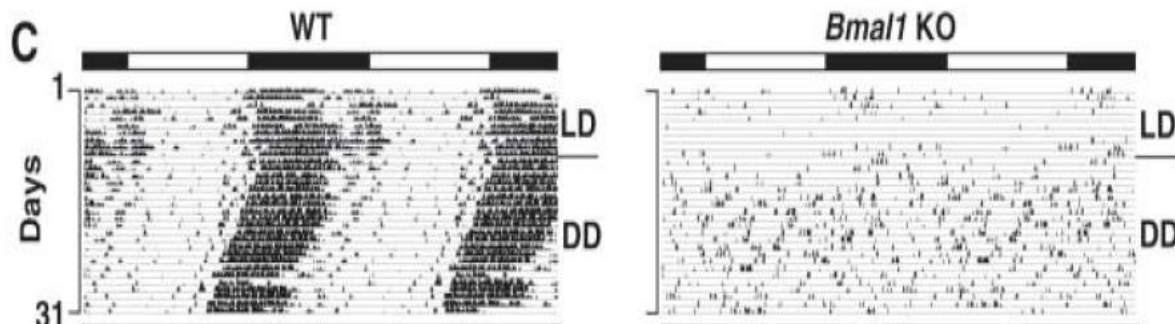
J.C. Ehlen et al., "Bmal1 function in skeletal muscle regulates sleep," *eLife*, 6:e26557, 2017.

ABOVE: © ISTOCK.COM, UNOL

### UPSIDE DOWN

The protein Bmal1, which helps regulate the body's internal clock, is found in especially high levels in the brain and in skeletal muscles. Mice completely deficient in Bmal1 were known to suffer from sleep impairments, but the specifics at play weren't clear. At the University of California, Los Angeles, Ketema Paul and colleagues looked to these mice for clues about the role Bmal1 plays in sleep regulation.

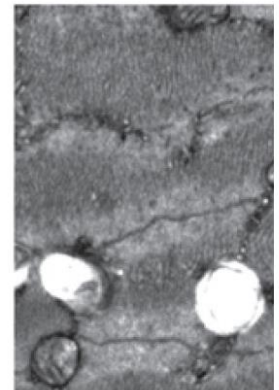
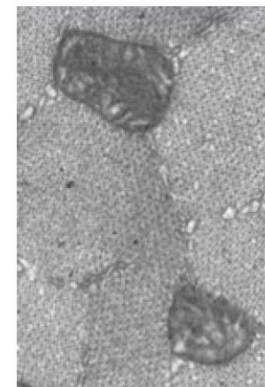
## Daily activity



## Mitochondria

Wildtype

*Bmal1* KO





# Sleep Loss and the Inflammatory Response in Mice Under Chronic Environmental Circadian Disruption

Allison J. Brager<sup>§</sup>, J. Christopher Ehlen<sup>§</sup>, Oscar Castanon-Cervantes, Divya Natarajan, Patrick Delisser, Alec J. Davidson, Ketema N. Paul\*

Department of Neurobiology, Morehouse School of Medicine, Atlanta, Georgia, United States of America

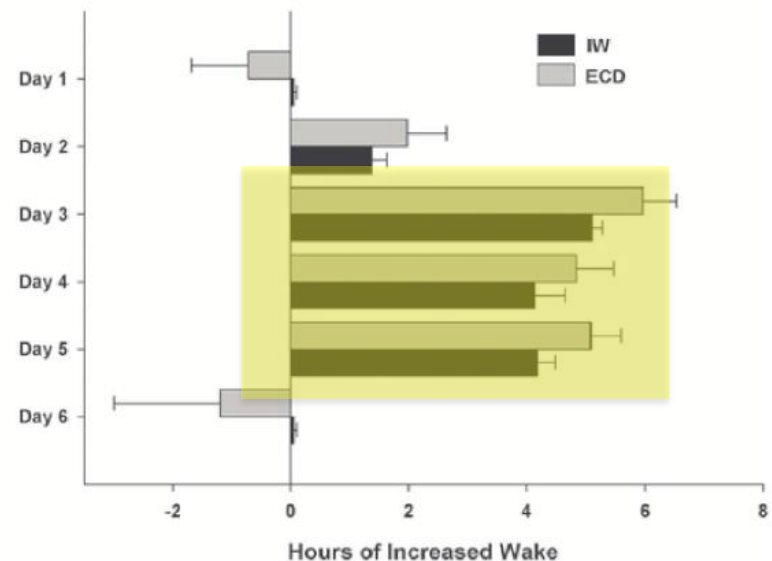
A.

	Hours			
	0-6	6-12	12-18	18-24
Baseline				
Shift 1				
Shift 2				
Shift 3				
Shift 4				



Cytokine levels

B.



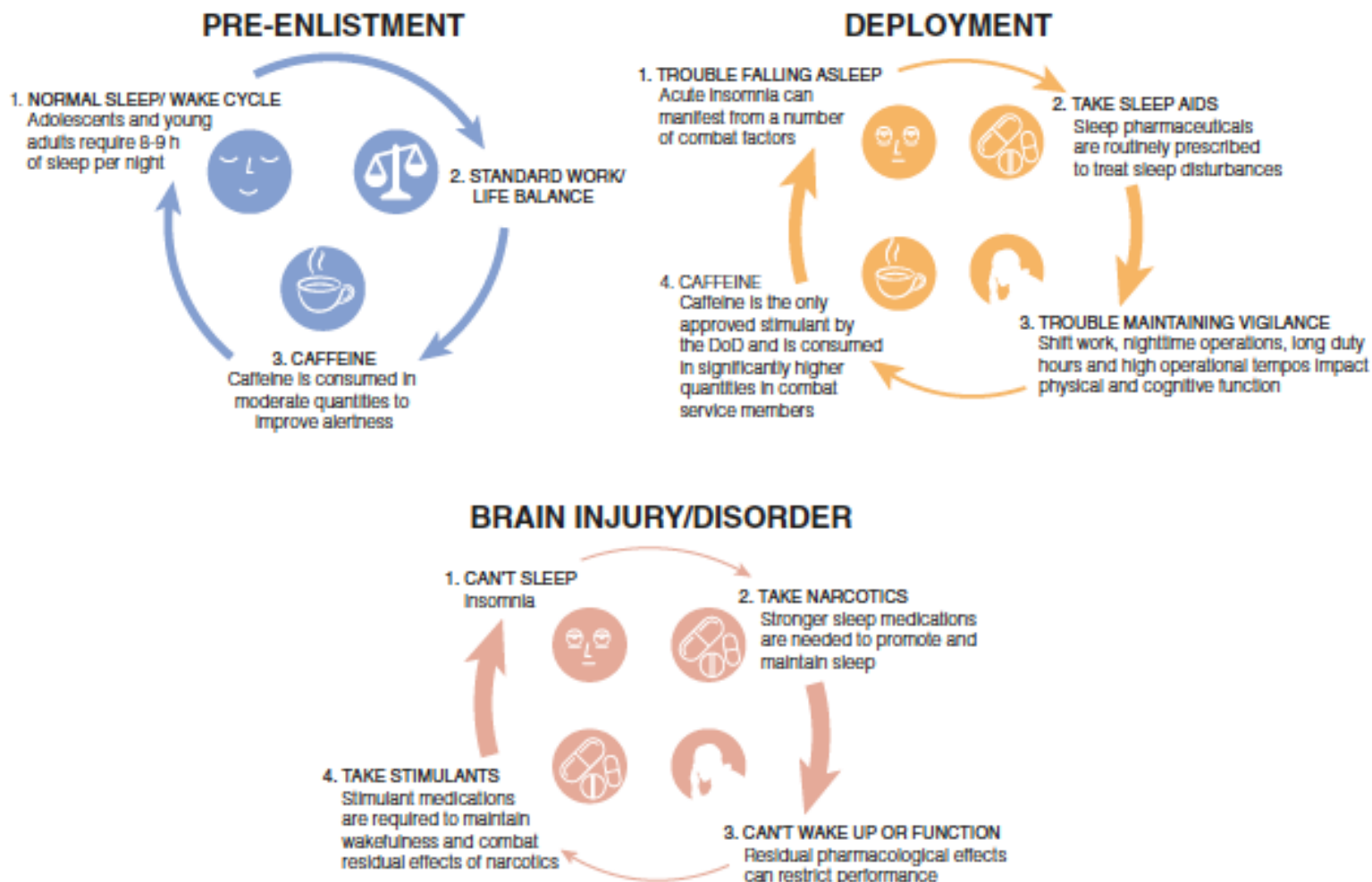
Immunological effects of shift work  
in healthcare workers

Bette Losf<sup>1,2</sup>, Nening M. Nanlohy<sup>1</sup>, Ronald H. J. Jacobi<sup>1</sup>, Chantal van de Ven<sup>4</sup>, Rob Mariman<sup>1</sup>, Allard J. van der Beek<sup>1</sup>, Karin I. Proper<sup>1\*</sup> & Debbie van Baarle<sup>1,3</sup>

SCIENTIFIC  
REPORTS  
nature research

# Sleep in the United States Military

Cameron H. Good<sup>1</sup>, Allison J. Brager<sup>2</sup>, Vincent F. Capaldi<sup>3</sup> and Vincent Mysliwiec<sup>4</sup>



**How to optimize nighttime sleep and waking performance?**

# How to maximize restorative sleep

## 1. Practice consistent sleep hygiene

## 2. Sleep timing matters

- Later to Bed: less NREM
- Earlier to Rise: less REM

## 3. Set “sleep goals”

- Sleep Diary (National Sleep Foundation)
- Wearables\*\*\*

Time pre-bed	“Activity”
90 min	No more work
60 min	No more phone
30 min	Low level activity (dim)
0 min	Dark, cool room

# Caffeine dosing strategies

	Optimal Caffeine	Energy Drinks:
Amount	< 200 mg/time	Monster: 240 mg Rockstar: 240 mg Bang: 300 mg
OPTEMPO < 24 h	4- 6 hours/ stop at 1800	
OPTEMPO > 24 h	4 -6 hours, as needed	

## Military Culture

### The military's obsession with energy drinks is contributing to PTSD, study finds

By: [J.D. Simkins](#)

October 26, 2018



# Napping strategies

LETTER TO THE EDITOR

## Challenging the stigma of workplace napping

Sara E. Alger<sup>\*,</sup>, Allison J. Brager and Vincent F. Capaldi

Behavioral Biology Branch, Walter Reed Army Institute of Research, Silver Spring, MD

“Why Should Someone Get Paid to Sleep on the Job?”

“I Don’t Have Time to Nap. I Have Too Much Work.”

“You Must be Lazy if You Take Naps.”

## Scientists agree: Coffee naps are better than coffee or naps alone

By Joseph Stromberg | Updated Apr 23, 2015, 8:45am EDT

Now, caffeine doesn't block every single adenosine receptor — it competes with adenosine for these spots, filling some, but not others.

But here's the trick of the coffee nap: sleeping **naturally clears adenosine** from the brain. If you nap for longer than 15 or 20 minutes, your brain is more likely to enter **deeper stages of sleep** that take some time to recover from. But shorter naps **generally don't lead to this** so-called **"sleep inertia"** — and it takes around 20 minutes for the caffeine to get through your gastrointestinal tract and bloodstream anyway.

So if you nap for those 20 minutes, you'll reduce your levels of adenosine just in time for the caffeine to kick in. The caffeine will have less adenosine to compete with, and will thereby be even more effective in making you alert.

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*IT TAKES ABOUT 20  
MINUTES FOR CAFFEINE  
TO HIT YOUR BRAIN*

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# Cost vs benefit of existing sleep/wake meds

Drug (recommended dose)	Half Life	Best Use			Side Effects	Considerations				Avoid				
		Promotes Sleep	Dedicate 7-8hrs of Sleep	Promotes Alertness		CNS Depressant	Anterograde Amnesia	Headaches	Increased Risk for Parasomnias	Abuse Potential	Black Box Warnings	Pregnancy Category	Present in Breast Milk Less Effective	Alcohol
 <b>ARMODAFINIL</b> Nuvigil 150mg	~15 h	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/> <input type="radio"/> <input checked="" type="radio"/> <input type="radio"/>	<input checked="" type="radio"/> <input type="radio"/> <b>C</b> <input type="radio"/> <input checked="" type="radio"/>	<input checked="" type="radio"/> <input type="radio"/> <b>C</b> <input type="radio"/> <input checked="" type="radio"/>	<input checked="" type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/>	<input checked="" type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/>					
 <b>MODAFINIL</b> Provigil 200mg	15 h	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/> <input type="radio"/> <input checked="" type="radio"/> <input type="radio"/>	<input checked="" type="radio"/> <input type="radio"/> <b>C</b> <input type="radio"/> <input checked="" type="radio"/>	<input checked="" type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/>	<input checked="" type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/>	<input checked="" type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/>					
  <b>CAFFEINE*</b> 200mg	~5 h	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/>	<input type="radio"/> <input type="radio"/> <b>A</b> <input checked="" type="radio"/> <input type="radio"/>	<input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/>	<input type="radio"/> <input checked="" type="radio"/> <input type="radio"/> <input type="radio"/>	<input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/>					
 <b>MIRTAZAPINE</b> Remeron 15- 45mg	20 - 40 h	<input checked="" type="radio"/> <input type="radio"/> <input type="radio"/>	<input checked="" type="radio"/> <input type="radio"/> <input type="radio"/>	<input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/>	<input checked="" type="radio"/> <input type="radio"/> <input checked="" type="radio"/> <input type="radio"/>	<input type="radio"/> <input checked="" type="radio"/> <b>C</b> <input checked="" type="radio"/> <input type="radio"/>	<input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/>	<input checked="" type="radio"/> <input checked="" type="radio"/> <input type="radio"/> <input type="radio"/>	<input checked="" type="radio"/> <input checked="" type="radio"/> <input type="radio"/> <input type="radio"/>					
 <b>LORAZEPAM</b> Ativan 0.5-2mg	~12 h	<input checked="" type="radio"/> <input checked="" type="radio"/> <input type="radio"/>	<input checked="" type="radio"/> <input type="radio"/> <input type="radio"/>	<input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/>	<input checked="" type="radio"/> <input checked="" type="radio"/> <input type="radio"/> <input type="radio"/>	<input checked="" type="radio"/> <input checked="" type="radio"/> <b>D</b> <input checked="" type="radio"/> <input type="radio"/>	<input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/>	<input checked="" type="radio"/> <input checked="" type="radio"/> <input type="radio"/> <input type="radio"/>	<input checked="" type="radio"/> <input checked="" type="radio"/> <input type="radio"/> <input type="radio"/>					
  <b>SUVOREXANT</b> Belsomra 10-20mg	~12 h	<input checked="" type="radio"/> <input checked="" type="radio"/> <input type="radio"/>	<input checked="" type="radio"/> <input type="radio"/> <input type="radio"/>	<input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/>	<input checked="" type="radio"/> <input type="radio"/> <input checked="" type="radio"/> <input checked="" type="radio"/>	<input checked="" type="radio"/> <input type="radio"/> <b>C</b> <input type="radio"/> <input type="radio"/>	<input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/>	<input checked="" type="radio"/> <input checked="" type="radio"/> <input checked="" type="radio"/> <input checked="" type="radio"/>	<input checked="" type="radio"/> <input checked="" type="radio"/> <input type="radio"/> <input type="radio"/>					
 <b>ALPRAZOLAM</b> Xanax 0.5mg	~11.2 h	<input checked="" type="radio"/> <input checked="" type="radio"/> <input type="radio"/>	<input checked="" type="radio"/> <input type="radio"/> <input type="radio"/>	<input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/>	<input checked="" type="radio"/> <input checked="" type="radio"/> <input type="radio"/> <input type="radio"/>	<input checked="" type="radio"/> <input checked="" type="radio"/> <b>D</b> <input checked="" type="radio"/> <input type="radio"/>	<input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/>	<input checked="" type="radio"/> <input checked="" type="radio"/> <input type="radio"/> <input type="radio"/>	<input checked="" type="radio"/> <input checked="" type="radio"/> <input type="radio"/> <input type="radio"/>					
 <b>TRAZODONE</b> Desyrel 50-100mg	5 - 9 h	<input checked="" type="radio"/> <input type="radio"/> <input type="radio"/>	<input checked="" type="radio"/> <input type="radio"/> <input type="radio"/>	<input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/>	<input checked="" type="radio"/> <input type="radio"/> <input checked="" type="radio"/> <input type="radio"/>	<input type="radio"/> <input checked="" type="radio"/> <b>C</b> <input checked="" type="radio"/> <input type="radio"/>	<input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/>	<input checked="" type="radio"/> <input checked="" type="radio"/> <input checked="" type="radio"/> <input checked="" type="radio"/>	<input checked="" type="radio"/> <input checked="" type="radio"/> <input type="radio"/> <input type="radio"/>					
 <b>ESZOPICLONE</b> Lunesta 1-3mg	~6 h	<input checked="" type="radio"/> <input checked="" type="radio"/> <input type="radio"/>	<input checked="" type="radio"/> <input type="radio"/> <input type="radio"/>	<input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/>	<input checked="" type="radio"/> <input type="radio"/> <input checked="" type="radio"/> <input checked="" type="radio"/>	<input checked="" type="radio"/> <input type="radio"/> <b>C</b> <input type="radio"/> <input type="radio"/>	<input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/>	<input checked="" type="radio"/> <input checked="" type="radio"/> <input checked="" type="radio"/> <input checked="" type="radio"/>	<input checked="" type="radio"/> <input checked="" type="radio"/> <input type="radio"/> <input type="radio"/>					
 <b>RAMELTEON</b> Rozerem 8mg	1 - 2.6 h	<input checked="" type="radio"/> <input type="radio"/> <input type="radio"/>	<input checked="" type="radio"/> <input type="radio"/> <input type="radio"/>	<input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/>	<input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/>	<input type="radio"/> <input type="radio"/> <b>C</b> <input type="radio"/> <input type="radio"/>	<input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/>	<input checked="" type="radio"/> <input checked="" type="radio"/> <input checked="" type="radio"/> <input checked="" type="radio"/>	<input checked="" type="radio"/> <input checked="" type="radio"/> <input type="radio"/> <input type="radio"/>					
 <b>ZOLPIDEM+</b> Ambien 5-10mg	~2.5 h	<input checked="" type="radio"/> <input checked="" type="radio"/> <input type="radio"/>	<input checked="" type="radio"/> <input type="radio"/> <input type="radio"/>	<input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/>	<input checked="" type="radio"/> <input type="radio"/> <input checked="" type="radio"/> <input checked="" type="radio"/>	<input checked="" type="radio"/> <input type="radio"/> <b>C</b> <input checked="" type="radio"/> <input type="radio"/>	<input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/>	<input checked="" type="radio"/> <input checked="" type="radio"/> <input checked="" type="radio"/> <input checked="" type="radio"/>	<input checked="" type="radio"/> <input checked="" type="radio"/> <input type="radio"/> <input type="radio"/>					
  <b>ZALEPLON</b> Sonata 5-20mg	~1 h	<input checked="" type="radio"/> <input checked="" type="radio"/> <input type="radio"/>	<input checked="" type="radio"/> <input type="radio"/> <input type="radio"/>	<input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/>	<input checked="" type="radio"/> <input type="radio"/> <input checked="" type="radio"/> <input checked="" type="radio"/>	<input checked="" type="radio"/> <input type="radio"/> <b>C</b> <input checked="" type="radio"/> <input type="radio"/>	<input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/>	<input checked="" type="radio"/> <input checked="" type="radio"/> <input checked="" type="radio"/> <input checked="" type="radio"/>	<input checked="" type="radio"/> <input checked="" type="radio"/> <input type="radio"/> <input type="radio"/>					
  <b>MELATONIN*</b> 0.3-3mg	30 - 50 m	<input checked="" type="radio"/> <input type="radio"/> <input type="radio"/>	<input checked="" type="radio"/> <input type="radio"/> <input type="radio"/>	<input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/>	<input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/>	<input type="radio"/> <input type="radio"/> <b>?</b> <b>?</b> <input type="radio"/>	<input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/>	<input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/>	<input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/>					



# Highlighted medications

- ★ **Caffeine:** Enhances alertness, vigilance, and physical endurance  
Avoid > 200 mg at a time (no energy drinks!) to reduce tolerance
- ★ **Suvorexant:** Latest sleep medication for insomnia. Targets a specific brain pathway controlling sleep-wake transitions, reducing feeling of next-day drowsiness common of “Z” drugs
- ★ **Zaleplon:** A “Z” drug with a short-half life reducing possibility of next-day drowsiness. Ideal for helping to fall asleep after late night game/game day travel
- ★ **Melatonin:** Safe, effective, and ideal for game day travel to help re-adjust to new time zone



# Concluding Remarks and Best Practices

- Lack of sleep is a crutch. Work smarter, not harder.
- Sleep smarter, not harder. Go to bed early. Utilize naps during high stress.
- Use caffeine strategically. No energy drinks!
- Don't be invincible. If you think you have a sleep disorder, get a sleep study.
- Questions? Ask me anything (@docjockzzz).