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## Sleep

**DISCLAIMER: the following is not meant to treat anyone with advice or tell you what you should do, such as relative to use of medication, exercise, or changing your diet. The information in this handout is merely offering what has been published in the research literature, as well as based on my professional experience. Talk to a doctor or other appropriate professionals as to what is best for your own specific needs.**

**It should also be appreciated that everyone has their own perspective on how to improve health. Nutritionists do it through food. Physicians do it through medicine. Psychologists do it through changing thoughts, feelings, and behaviors. Consequently, what is offered here is a reflection of my own bias and perspective.**

*“Sleep is the chief nourisher in life’s feast.” – Macbeth, William Shakespeare*

Recommended sleep duration times, by age

Age	Recommended	Appropriate	Not recommended
<b>0-3 months</b>	14 to 17 hours	11 to 13 hours, 18 to 19 hours	<11 hours, >19 hours
<b>4-11 months</b>	12 to 15 hours	10 to 11 hours, 16 to 18 hours	<10 hours, >18 hours
<b>1-2 years</b>	11 to 14 hours	9 to 10 hours, 15 to 16 hours	<9 hours, >16 hours
<b>3-5 years</b>	10 to 13 hours	8 to 9 hours, 14 hours	<8 hours, >14 hours
<b>6-13 years</b>	9 to 11 hours	7 to 8 hours, 12 hours	< 7 hours, >12 hours
<b>14-17 years</b>	8 to 10 hours	7 hours, 11 hours	<7 hours, >12 hours
<b>18-25 years</b>	7 to 9 hours	6 hours, 10 to 11 hours	<6 hours, >11 hours
<b>26-64 years</b>	7 to 9 hours	6 hours, 10 hours	<6 hours, >10 hours
<b>65+ years</b>	7 to 8 hours	5 to 6 hours, 9 hours	<5 hours, > 9 hours

Taken from the National Sleep Foundation, and “scientifically grounded guidelines on the amount of sleep we need each night to improve the sleep health of the millions of individuals and parents who rely on us for this information.” Charles Czeisler, PhD, MD

What keeps us most healthy? Getting regular exercise? A good, healthy diet? Adequate sleep? How long can you stay alive and healthy if you forego exercise temporarily? Months for sure. How long can you remain pretty energetic and healthy with no food intake? Several days, maybe a week. How long can you go without sleep before it catches up to you? Twenty-four hours is stretching it. Now reconsider, what keeps us most healthy?

Questions were asked of people in Spain, Greece, Australia, Germany, Israel, Japan, S. Korea, and Canada: ‘What type of health and wellness education did you receive when you were in school?’ Instruction on diet was received by 98%. Drugs, alcohol, and safe sex? 87%. Exercise? 100%. Sleep: 0%.

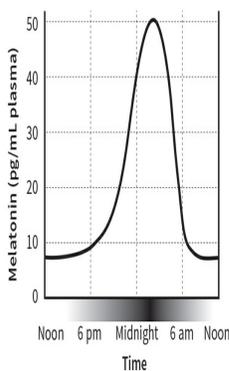
So for all of you who have never received any education on the importance of sleep, read on please.

**Sleep rule #1: the only way to truly get rid of sleepiness is to sleep.**

**Sleep rule #2: there is no sleep bank.** (e.g. You can't sleep poorly on weekdays, and catch up on weekends. Damage is done.)

A key cellular fuel for us is ATP, adenosine triphosphate. In brain metabolism adenosine is broken off and the chemical accumulates, creating what is called sleep pressure. As long as you remain awake it continues to build, making you ever more tired and pushing you toward wanting sleep.

Everyone knows that caffeine reduces sleepiness, and it does this by blocking the receptor sites that adenosine fits into in the brain. Consequently, the adenosine is present but the signal for sleep is not being received. However, caffeine wears off eventually. And all the while caffeine is keeping you more awake and alert the adenosine has continued to build. Once the caffeine is gone there is even more adenosine that has piled up inside of your brain, creating even greater sleep pressure, resulting in what some call having a caffeine crash. So, the only way to get rid of adenosine is to sleep.

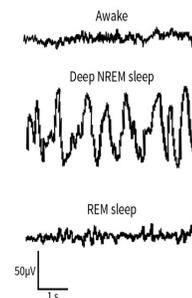


There is another factor that helps regulate our sleep patterns which is the circadian rhythm which includes the release of melatonin, a hormone involved with sleep. Sleep pressure and the circadian rhythm are not linked together. Ideally they coincide with each other. But consider what happens when you fly across time zones and have jet lag? Or pull an all nighter studying or working, or caring for a sick child? Stay up too long and you will feel the fatigue as sleep pressure builds, but then you discover a second wind – as melatonin is decreasing in the morning hours and you feel more alert again. Adenosine is still building up in your brain but it is being countered by your circadian rhythm to some extent.

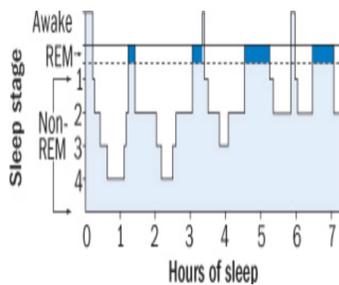
Why we sleep, Matthew Walker

Sleep serves many functions, and they are derived from the different states of sleep. We all know of being in a light vs. deeper state of sleep. We also know that for part of our sleep we are dreaming, and other times we are not. So let's use some descriptive labels to keep the ideas that are offered in the following pages clear.

These are tracings from an EEG machine recording brain waves. One way to differentiate the states of sleep is through a stage called rapid eye movement (REM, where your eyes move rapidly under your eyelids) which is where the bulk of dreaming occurs, and especially the bizarre types we all have experienced. There is also non-REM (NREM) sleep, which is self-explanatory as to what it entails. Different stages of NREM exist, and stage 4 is deepest and more difficult to awaken from than earlier ones. Stage 1 is where you still have some awareness, meaning it is a very light sleep, and you may not even realize you have been asleep.



Why we sleep, Matthew Walker



Harvard Health Publishing, "Repaying your sleep debt" 5/9/2018

REM and NREM play a zero-sum game across our sleep. When one increases the other naturally decreases. The graph to the left shows a single night's stages of sleep. Early on there is a lot of NREM, and little REM. Shortly before waking up this reverses, and REM predominates. How much of each occurs at different stages of our life from fetus through our older years varies greatly. Each of these sleep types plays different roles. Both are important. Mother Nature does stuff for reasons.

Think of Michelangelo taking a hunk of marble and creating some masterpiece statue from it. How did he start? Cutting away large swaths of unneeded material. But what he is known for is not the removal of waste, but the chiseling of fine detail, the artistic side of his genius. NREM sleep is the large removal of waste, getting rid of the nonessential from our day's experience. In computer terms it is deleting non-essential files, getting rid of clutter that is no longer needed.

REM sleep is the opposite. It saves important memories, and it basically is creating file folders and cross-links so that we can retrieve that information when needed. It also serves another purpose that we can call creativity, or being insightful. Paul McCartney's 'Yesterday' was composed in one of his dreams. Einstein's understanding the theory of relativity, came to him in a dream.

This pattern of 'first NREM, and then REM sleep' creates hazards for our health if we have an inadequate amount of sleep. Shortchange the earlier hours, and NREM is lost. Lose the later hours of sleep and REM is mostly foregone. There are health consequences for both of these omissions.

One element of NREM is the presence of 'sleep spindles' that is an extra electrical activity on the downbeat of the slow wave NREM cycle. Sleep spindles occur both in light and deep NREM, and especially in the transition from NREM to REM. One function they serve is to shield the brain from external noise, so that more powerful and frequent sleep spindles make a person more resilient to being awoken from noise around them.

Sleep spindles have another purpose, which is to help with learning and memory. Sleep spindles help take information out of short term memory storage and put it into long term. In computer terms, this is taking information out of the limited amount of RAM memory you have, and sticking it onto the hard drive that is far greater in size. Clear out the short term and you can then put something else there, learning anew.

One research study took pianists and taught them a pattern of certain notes to be played as quickly and accurately as possible. One group was given twelve minutes to learn the pattern, and then re-tested after twelve hours, later that evening. The other group learned the pattern in 12 minutes in the evening, got a full night of sleep, and was tested twelve hours later the next day. The first group had no change in performance when tested. The group that slept was 20% faster and almost 35% more accurate. The first group caught up – after they had gotten a night's worth of sleep. Brain scanning research has found that it is stage 2 NREM sleep, from hours 5-7 out of an eight hour sleep cycle, and the number of sleep spindles occurring then that is linked to this boost in memory and performance. The sleep spindles that arose in this study were in the area that involves motor control. Another example was done with rats who were running a maze

during the time. At night their brains lit up in the motor cortex during NREM sleep, with the memories being played forward and backward but at ten times the normal speed that they had in fact run it. A broader example: stage 2 NREM spikes around the age when infants go from crawling to walking, when a great deal of motor development is obviously occurring.

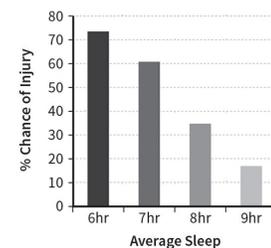
Another study looked at what is called declarative memory (e.g. facts and figures learned in school) and sleep spindles' role in it. They took college students and one group was given normal sleep at night while the others were kept awake. The next day they were given a list of facts to learn, and then they were given two nights of normal sleep, so that the sleep deprivation was only occurring while learning and not while recalling the information. When tested after the two nights the sleep deprived group were 40% weaker in their ability to learn relative to those who had slept the first night. This would be like getting a 100 vs. a 60 on a test, acing vs. failing. NREM stage 3 was more involved with this learning. **Sleep rule #2:** memories formed without sleep are weaker, and evaporate faster. This is why cramming for tests does not see such material 'stick.'

Other research that has been going on for decades looked at identical twins, with one getting more sleep than the other. By the age of 10 years the longer sleeping twin was superior in intelligence and educational abilities with higher scores on standardized tests of reading and comprehension, and a bigger vocabulary than the twin who slept less.

The International Olympic Committee as of 2015 published a statement saying that sleep is critical for athletes. Professional sports teams are taking notice too. Over 750 research studies have been done on this subject. Findings include that less than eight hours of sleep in athletes, and especially under six hours leads to:

- ❖ a 10-30% drop in time to physical exhaustion
- ❖ aerobic output is significantly reduced
- ❖ decreases in peak and sustained muscle strength
- ❖ reduced cardiovascular, metabolic and respiratory capabilities
- ❖ lower blood oxygen saturation
- ❖ less ability of the body to cool itself through sweating
- ❖ increased risk of injury

Figure 10: Sleep Loss and Sports Injury

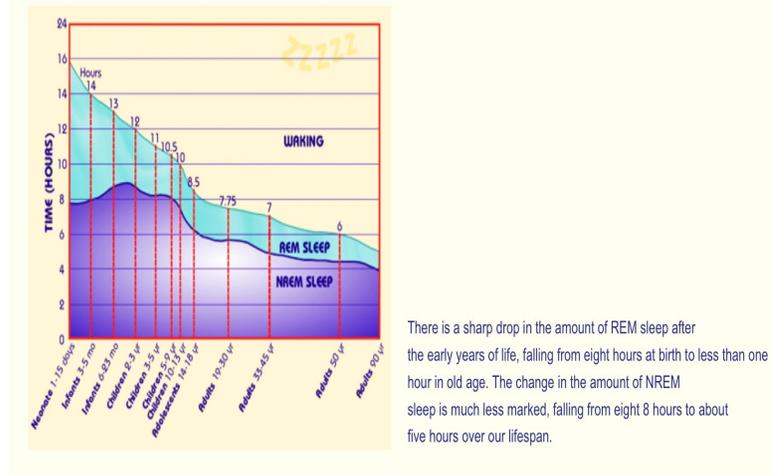


Why we sleep. Matthew Walker

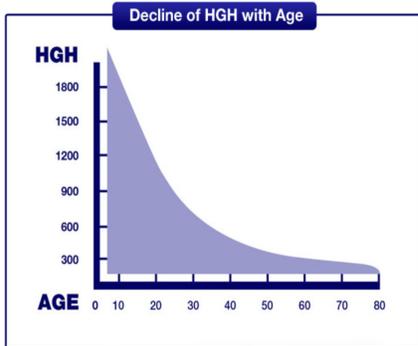
Sleep spindles decrease with aging. People who are 60-80 years old have been found to have 40% fewer sleep spindles – and they have reduced ability to learn the next day upon awakening so there is less memorization capability. We all know that getting older brings with it less ability to learn and remember information. This lack of sleep spindles is one reason why.

[http://www.habitot.org/hab/newsletter/sleep/sleep\\_over\\_the\\_lifespan\\_nrem\\_rem\\_ratio.html](http://www.habitot.org/hab/newsletter/sleep/sleep_over_the_lifespan_nrem_rem_ratio.html)

Over the course of our life span sleep patterns change dramatically to meet our changing needs, as the graph to the left shows. Older individuals often get less than they need to because of sleep related neurons in the hypothalamus which may be related to the circadian rhythm dying off.



One of the health consequences of cutting sleep short in the hours closer to awakening is that sleep spindles are especially rich in number then. Lose them, and you are more forgetful, because information is not being stored as well in long term memory.



<https://fitness.mercola.com/sites/fitness/archive/2013/02/01/whey-protein-improves-hgh.aspx>

Human growth hormone (HGH) beyond making kids grow is also involved in repair. Some estimates are that up to 75% of HGH is released during sleep especially in stage 3 NREM. Exercise perhaps especially high intensity interval training can also trigger its release, as may intermittent fasting. Sleep deprivation or disruption also can lower HGH. High sugar intake boosts insulin, which lowers HGH, so if you need another reason to stay away from sugar, add this one.

So, you think that during sleep nothing is happening other than you are asleep, and you dream? Look at this graphic to get a partial clue as to the complexity of what is going on while you sleep.

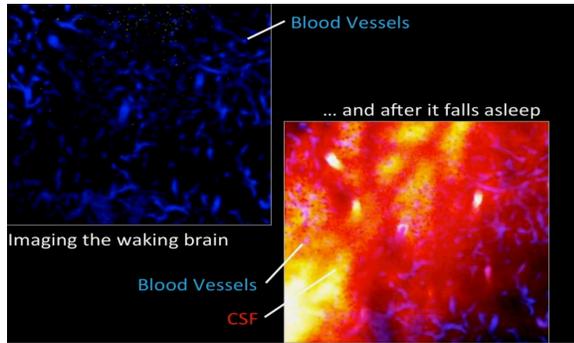
“Chemical messengers: how hormones help us sleep,” 9/5/2015  
<http://theconversation.com/chemical-messengers-how-hormones-help-us-sleep-44983>

### Hormones released in the brain during sleep

- Growth hormone:**
  - > Essential for growth and tissue repair
  - Produced in the pituitary gland (in the brain)
  - Released during sleep
- Antidiuretic hormone (ADH):**
  - > Prevents the production of dilute urine
  - Produced in the pituitary gland (in the brain)
  - Levels of ADH increase during sleep
- Melatonin:**
  - > Signals to the body that it is time to sleep
  - Produced in the pineal gland (in the brain)
  - Released with increased darkness
- Oxytocin:**
  - > Involved in childbirth, lactation and social behaviour
  - Produced in the hypothalamus (base of the brain)
  - Levels peak after 5 hours of sleep
  - Levels may influence the content of dreams
- Prolactin:**
  - > Involved in over 300 functions including lactation, metabolism and immune system regulation
  - Produced in the pituitary gland
  - Levels are higher during sleep than in daytime

Which type of sleep, NREM or REM is more important? If people are deprived of sleep their brain will feast for the first night of recovered sleep on NREM. Subsequent nights it packs on more REM.

### What bad results occur from inadequate sleep? Lots!



One more reason to get a good night's sleep. Jeff Iliff. <https://youtu.be/MJK-dMIATmM>

One purpose of sleep is it is a time for the brain to be cleaned of waste products, like adenosine, so that we are not sleepy upon awakening assuming we get enough hours of shut eye. But other waste products also are building up in the brain such as the plaque that is associated with Alzheimer's. During sleep glial cells of the brain shrink by up to 60% to make room for cerebrospinal fluid (CSF) to be pumped along the outside of the brain's blood vessels to clean out the day's waste.

A single night of bad sleep raised amyloid beta plaque, while a week's worth increased tau protein – another culprit that is related to Alzheimer's. These two building up in the brain causes brain tissue to degenerate and die, and also correlates with progression of Alzheimer's.

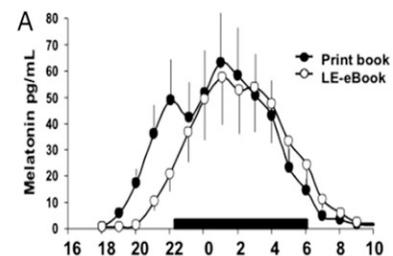


Use of electronic books late at night also has been studied as to their impact on sleep. One study's finding was that they reduced the amount of melatonin secreted by an average of 55%, plus shifted it 1.5 hours later compared to reading a print book in bed. The graph below shows what happens after five days of e-reading with a sleep time of 10/P to 6/A.

Harvard Health Publishing, "Blue light has a dark side" 8/13/2018

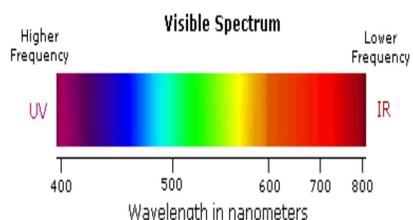
Evening use of light-emitting eReaders negatively affects sleep, circadian timing, and next morning alertness." Anne-Marie Chang et al.

Sleep onset was on average ten minutes longer for e-book readers vs. print. REM sleep was significantly reduced by about twelve minutes, which may affect sleepiness upon awakening. Total sleep time and NREM sleep were the same for both types of readers. E-readers rated themselves as less sleepy an hour before bedtime. In the morning they rated themselves more sleepy. It also took them hours longer to fully 'wake up' and attain the same level of alertness compared to print readers. Also, by shifting melatonin to a later hour there is an impact on circadian rhythm which can create chronic sleep onset insomnia.

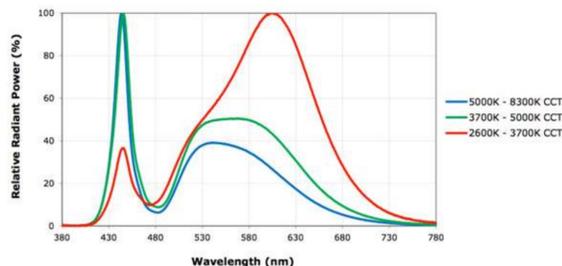


Similar research on e-books was done by Brigham & Women's Hospital in Boston, with comparable results. They also found that use of the e-books increased cortisol which is a daytime hormone that is stimulating in its effects.

JAMA Pediatrics published a meta-analysis of 20 studies involving 125,198 kids ranging between 6-19 years old with an average age of 14.5 years looking at cell phone and tablet usage and their impact on sleep (excluding tv and computer usage). They found a "consistent association" between using smart phones and tablets before bedtime and inadequate sleep quantity, poor sleep quality, and being excessively sleepy during the day.



- Violet: 400 - 420 nm
- Indigo: 420 - 440 nm
- Blue: 440 - 490 nm
- Green: 490 - 570 nm
- Yellow: 570 - 585 nm
- Orange: 585 - 620 nm
- Red: 620 - 780 nm



<https://www.digikey.com/en/articles/techzone/2013/apr/defining-the-color-characteristics-of-white-leds>

Warm white=2700-3000K Cool white=3500-4100K.

Daylight=5000-6500K.

<https://www2.chemistry.msu.edu/faculty/reusch/virttxtjml/spectry/uv-vis/spectrum.htm>

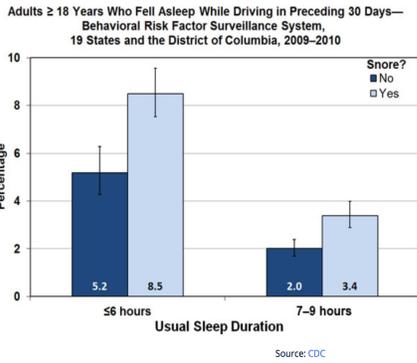
The graphics above are a way of capturing another hazard to your sleep, namely use of ordinary light bulbs. There are different temperature bulbs, which are classified as ‘warm,’ ‘cool,’ and ‘natural/daylight.’ The graph on the far right shows that cool and daylight bulbs put out a lot of blue light down around 450 nm. Warm white bulbs have little blue to them, and instead a lot of reddish-orange, and are more like the tint of incandescent lights.

Research done at Rensselaer Polytech found that the melatonin system is sensitive to 440-460 nm light, meaning where a lot of current energy efficient bulbs such as compact fluorescent and LEDs are functioning. Another study done in Switzerland in 2005 found that human volunteers exposed to two hours of 460 nm light at night experienced about 60% melatonin suppression vs. light at 550 nm which is in the yellow-green spectrum. Research done by Harvard compared 6.5 hours of blue light vs. green. The blue suppressed melatonin for about twice as long, and shifted the circadian rhythm by twice as much, 3 vs. 1.5 hours. How bright does indoor light at night have to be to suppress melatonin? There is diversity of opinion. Some research has found that as little as 8 lux (about the power of two night lights) can have an impact.

What does this all suggest? Avoiding use of electronic screens at night to prevent melatonin suppression may be inadequate if your interior lights are cool white or daylight temperature bulbs. But even low level incandescent light bulbs, with their reddish-orange cast, can cause problems. A review on the issue published in 2007 in the Journal of Pineal Research found that lighting through such bulbs for just thirty-nine minutes suppressed melatonin levels by up to 50%. So, at night too bright, too blue, or too long an exposure to light can cause problems.

### Motor vehicle crashes

People have known for a long time that drivers can fall asleep at the wheel, or be drowsy and have impaired reaction times, leading to crashes. No one knew with any accuracy how often such crashes occurred from being sleepy. Dead men tell no tales. e.g. If someone crashes while going around a curve at 70 MPH and dies it can be easily written off as being due to ‘excessive speed.’ If the driver survives they may not want to admit to being tired or sleepy and getting a ticket from the police for ‘driving to endanger’ or the like. Or, they may not know just how tired they were.



Crashes can also result from what is called microsleep where some parts of the brain are asleep but others remain awake. This can arise without the driver even knowing it meaning there is a selective loss of awareness. It may last a fraction of a second out to a few minutes. The driver may not respond to external stimuli like a red light, or a curve in the road. Sleep deprivation causes it, as does doing something repetitive like driving for long periods of time. People with insomnia or sleep apnea are also at higher risk.

“Microsleep” 4/12/2017 <https://www.tuck.com/microsleep/>

In the past estimates were that something like 1-2% of accidents were due to drowsy driving. The AAA released results of a study in early 2018 involving 4,000 vehicles that were equipped with a dash cam on the driver. Over the few months of the study there were over 700 accidents. They looked at the last three minutes of the dash cam footage and analyzed through use of a scientific gauge for signs of sleepiness. They found approximately 10% of the crashes were due to it. Based on such a rate, that would mean that drowsy driving is responsible for about 600,000 accidents a year in the U.S., 300,000 annual injuries, and about 3,500 annual deaths. However, other AAA research puts crashes with at least one hospitalized person happening 13% of the time from drowsy driving, and 17% of vehicular fatalities being related to it. Whatever the real numbers are, they are big, and are preventable. Trying to stay awake while driving tired by use of loud music, rolling down the window, slapping your face, etc.? Remember Sleep Rule #1- none of them work.

Age	Likelihood of being involved in a drowsy driving MVA
18-29	71%
30-64	52%
65+	19%

National Sleep Foundation, Drowsy Driving Facts & Stats. <http://drowsydriving.org/about/facts-and-stats/>

Shift workers are more likely than those working regular daytime hours to drive drowsy at least a few days a month (36% vs. 25%). Research in Australia found that being awake for 18 hours produced an impairment equal to having a blood alcohol level of .05, and being up for 24 hours was equal to a .10 blood alcohol. Drowsy driving can result in jail sentences for the driver, along with multi-million dollar settlements resulting to families of crash victims. Commercial drivers are especially at risk for drowsy driving. Various gadgets and apps have been created to detect drowsy driving (e.g. see <https://medium.com/vorm/technology-against-drowsy-driving-72ede9265b84>)

Other risk factors for drowsy driving include

- ❖ inadequate, interrupted or fragmented sleep
- ❖ driving for too long without sufficient rest periods
- ❖ use of sedatives, hypnotics or other sleep aids prior to driving
- ❖ consumption of alcohol or narcotics
- ❖ narcolepsy
- ❖ a work schedule that affects the amount of sleep and/or circadian rhythm

There is another side to drowsy driving that parents of teens probably know of. High schoolers are renowned for having a circadian rhythm different than just about anybody, with their going to bed maybe at midnight or 2 AM and until then being full of energy. High schools tend to start

around 7:30 AM and so such students are beyond sleep deprived on a daily basis. Car accidents are the leading cause of death for ages 16-19.

Some school districts have switched to a later start in the morning. Teton County, WY went from 7:35 AM to 8:55 AM and there was a 70% reduction in car crashes for ages 16-18. Mahtomedi school district in MN went from 7:30 to 8 AM for a start time, and 60% fewer crashes resulted among 16-18 year old students. ABS brakes in comparison led to a 20-25% reduction and that was considered a big deal.

### Heart disease

Every year the U.S. government helps foster a 25% increase in heart attacks on a single day – the one after Daylight Savings Time starts in the Spring. And in the Fall with an extra hour of sleep heart attacks decline by 21% the next day. The total number of heart attacks stays the same, meaning that the extra stress of that single lost hour on one night is just advancing when people have heart attacks. But what happens if you lose one or more hours of sleep a night for months, years, decades?

Greek culture used to be that business would be open from something like 9 AM to 1 PM, and then they would take a siesta to 5 PM, and re-open to 9 PM. In recent years they have become more business like, and started cutting out the mid-day nap and worked straight through to the late afternoon. Harvard's School of Public Health, looked at 23,000+ Greek adults where there used to be a siesta mid-day. None had a history of heart disease, and the age range was from 20-83 years old. They were tracked across a six year period, with some still taking the siesta and others stopping it. Those who abandoned the regular siesta had a 37% increased risk of death from heart disease over the six year period vs. those that maintained regular daytime naps. It was especially notable in working men who had a 60+% increased risk of dying.

An even larger study was done in 2011 that tracked more than 500,000 people of varying races, ethnicities and ages across eight countries. Progressively shorter sleep was associated with 45% increased risk of developing and/or dying from heart disease within 7-25 years from the study's start. A Japanese study of 4,000+ male workers done over fourteen years found those sleeping 6 hours or less had a 400-500% greater likelihood of having one or more heart attacks vs. those getting more than six hours. The simple explanation for such findings is that insufficient sleep stresses the body and engages the sympathetic nervous system ('fight or flight' response) and those stress hormones that are chronically elevated tax the cardiovascular system.

Deep NREM sleep in particular calms down this stress response and so help averts high blood pressure and strokes.

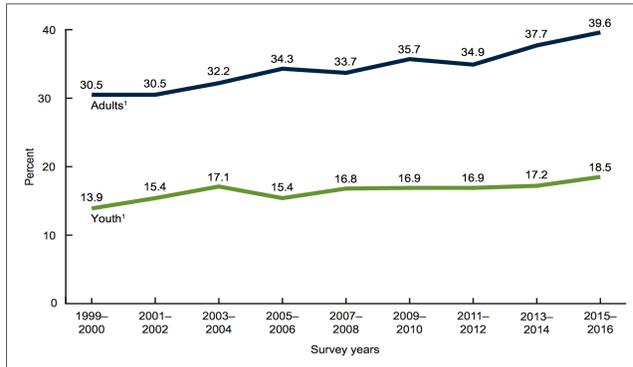
### Alzheimer's

Ten percent of people over the age of 65 have Alzheimer's. And sleep disruption can cause Alzheimer's. One of the areas of the brain where the amyloid plaque of Alzheimer's accumulates is a particular portion of the frontal lobe – and this area helps generate NREM sleep. The greater number of amyloid plaques there the greater impairment in deep sleep that has been found in older people, which included more forgetting rather than consolidating of memories that occurred over a night of sleeping. What results is a downward spiral: more plaques create less deep sleep. Less deep sleep means less effective cleansing of the plaques by way of the CSF, which means more plaque is left behind to accumulate.

It has been found that depriving mice of sleep increases beta amyloid levels. Infusing them with orexin, a hormone involved in wakefulness and appetite also increased amyloid. Injecting a drug that blocks orexin decreased such levels. This is the first evidence showing that if you manipulate the sleep/wake cycle that could potentially play a role in causing neurodegenerative disease (24).

## Obesity

Figure 5. Trends in obesity prevalence among adults aged 20 and over (age adjusted) and youth aged 2–19 years: United States, 1999–2000 through 2015–2016



Significant increasing linear trend from 1999–2000 through 2015–2016.  
NOTES: All estimates for adults are age adjusted by the direct method to the 2000 U.S. census population using the age groups 20–39, 40–59, and 60 and over.  
Access data table for Figure 5 at: [https://www.cdc.gov/nchs/data/databriefs/db258\\_table.pdf#5](https://www.cdc.gov/nchs/data/databriefs/db258_table.pdf#5).  
SOURCE: NCHS, National Health and Nutrition Examination Survey, 1999–2016.

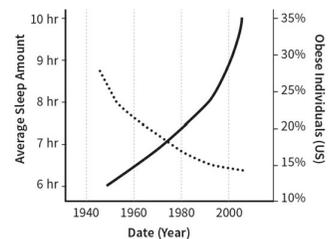
As of 2015–2016 the CDC said that 39.6% of U.S. adults were obese, affecting over 93 million. Kids ages 2–19 have an obesity rate of 18.5%, and even 2–5 year olds had a rate of 13.9% according to the CDC. And as you can see from the graph to the left, the trend has been getting worse over the last twenty years.

What are some possible reasons for this, and what can be done about it?

Here is one clue.

Epidemiological studies have established that people who get less sleep are the ones more likely to be overweight or obese. You can see this for yourself in the graph to the right that reflects the average sleep being obtained along with obesity rates measured over fifty years. Why we sleep. Matthew Walker

Figure 13: Sleep Loss and Obesity



There are various hormones that impact our eating behavior. They include ghrelin which turns on appetite, and leptin which tells us we have eaten enough and to stop doing so. Nature has perfected such a balance of hormones over millions of years of evolution. Tamper with the hormonal balance and bad stuff will inevitably happen.

One study took people in a controlled laboratory setting and gave them 8½ hours of sleep a night for five nights. They were also given just 4–5 hours a night. The exact same amount and type food, and degree of physical activity were held constant. Daily hunger and food intake were monitored along with circulating levels of ghrelin and leptin. Inadequate sleep increased ghrelin and decreased leptin, making the subjects eat an extra 300 calories/day compared to getting a full night of sleep. Scaled up across a year that would be about a thirty-one pound weight gain.

A similar experiment using that amount of sleep then offered the participants a four hour buffet on the last night with all manner of items from salads to ice cream, including lots of junk food like cookies, chips and pretzels. They were allowed to eat as much as they wanted during the four hours and they did so alone so there would be no stigmatizing influence that might influence their behavior. Despite eating a normal 2000 calories during the day the sleep deprived group added 330 more calories of snack food compared to those who got the full night's sleep.

What was discovered is that another hormone regulating sleep, endocannabinoids (similar to the chemical in marijuana which creates 'the mad munchies'), had been increased from the sleep

loss. The research also showed that such mad munchies did not make people want to eat something like carrot sticks or salmon fillets. Instead the participants were going for the junk food which had a 30-40% increase vs. 10-15% bump for protein rich foods.

Why does sleep deprived mad munchies make us go toward junk food? The participants were put in brain scanning machines and the prefrontal region (the most advanced part of the human brain, that gives us judgment, reasoning, morality, looking at pros and cons, etc.) gets turned off from inadequate sleep. What gets activated through sleep deprivation is the part of the brain that is involved with motivation and desire, the fun side of life, such as what tastes really good.

Animals studies have shown that the orexin system becomes overactive during sleep deprivation which can then lead to weight gain.

Greater amounts of prolactin are also produced during the day when there is inadequate sleep at night. And daytime prolactin secretion can lead to autoimmune problems and carb craving.

Another study took overweight males and females and studied them for two weeks in a medical center. One group got 5½ hours of sleep while the others got 8½ hours. Both groups lost weight on a strict, low calorie diet. But for the sleep restricted group over 70% of weight loss came from muscle and not fat. The full sleep group had more than half their weight loss come from fat.

Three year old kids getting only 10½ hours of sleep are now found to have a 45% greater risk of being obese by age 7 vs. those who get 12 hours of sleep/night.

### Diabetes

One study had healthy research participants get just four hours of sleep a night for six nights. They then were given a standard dose of glucose and looked at how their bodies absorbed and managed it as to keeping blood sugar at a healthy level. That lack of sleep made their bodies respond as if they were pre-diabetic, in that their cells had become more insulin resistant. The Nurses Health Study followed 70,000 non-diabetic women for ten years. Compared to those getting 7-8 hours in 24 hours, those with 5 hours or less sleep had a 34% greater risk of diabetes even after controlling for many variables such as BMI, shift work, high blood pressure, exercise and depression. A meta analysis of over 107K people followed for an average of 9.5 years found sleep under 5 or 6 hours led to a 28% higher risk of developing diabetes. Difficulties with falling asleep led to a 57% higher risk, and difficulties staying asleep created 84% more risk. Other research has found that in young, healthy men limited to four hours of sleep for six nights, and young healthy women limited to three hours for one night led to higher cortisol levels. Another study involving 2,751 men and women found that short sleep duration and sleep disturbances are independently associated with more cortisol secretion in the evening. And elevated cortisol levels can lead to morning insulin resistance.

Inflammation also increases with decreased sleep, and this too can increase insulin resistance.

Sleep deprivation also stimulates the sympathetic nervous system – which inhibits insulin release, and increases insulin resistance. The parasympathetic nervous system (the side that calms us down) stimulates insulin release.

Still another factor is that slow wave sleep is the most restorative form, and is associated with metabolic and hormonal changes that affect glucose balance. There have been a few small studies looking at what happens when slow wave sleep is suppressed as to the impact on glucose

balance. One took nine young, lean, non-diabetic men and women and looked at two nights of good undisturbed sleep, and three nights of consecutive suppressed slow-wave sleep, without a change in total sleep duration or in REM duration. Slow wave sleep was disrupted acoustically, and reduced by nearly 90%, and sleep fragmentation was comparable to what moderate to severe sleep apnea does. After three nights of slow wave suppression insulin sensitivity was cut by 25% without any extra insulin being released, and this resulted in a reduction of 23% in glucose tolerance.

Another study looked at sleep apnea. It involved 60 patients with type 2 diabetes and 77% had apnea (OSA). The worse the OSA the worse the glucose control. After controlling for age, sex, race, BMI, number of diabetes meds, level of exercise, years of diabetes, and total sleep time, there was a linear trend between A1C being significantly increased and the degree of OSA.

Degree of OSA	Increase in A1C
Mild	1.49%
Moderate	1.93%
Severe	3.69%

Another study on OSA found that use of CPAP attenuated risk of diabetes.

Bottom line: chronic sleep deprivation is now known to be one of the major contributors to type 2 diabetes.

### Immune System

Sleep boosts the immune system, and lack of sleep takes a toll on it. One experiment took 150 healthy men and women and measured their sleep for a week. There were four groups: those getting less than 5 hours of sleep/night, 5-6 hours, 6-7 hours, and 7 or more. They then had a cold virus squirted up their noses after that week of sleep. What was found was a linear relationship between limited sleep and coming down with a cold. For those getting under 5 hours almost 50% became sick. For 7+ hours the rate was just 18%.

A variation of this finding was made relative to the flu vaccine. The experiment had two groups of people: those limited to four hours of sleep vs. 8½ hours and done for six nights. At the end of the sixth day everyone was given a flu shot. In the following days blood samples were taken looking for how many antibodies were generated. Those getting the full sleep for six nights had a healthy and robust response. Those with less sleep had less than half that of their well rested counterparts. Similar findings have been found with vaccines for hepatitis A & B.

So you say, ‘Well, I’ll just get more sleep the week after the flu shot and that’ll get me caught up!’ Guess again. Even after a year the sleep deprived subjects still did not have a full response of certain immune cells. Remember **sleep rule #2?**

### Cancer

A weakened immune system has other consequences beyond the flu and common cold. One part of our immune system are called natural killer cells. These are cells that do not need to be exposed to something before they are turned on, they are ready to kill the first time they find a foreign invader. One of their targets are cancer cells. A single night of getting 4 hours of sleep reduced by 70% the number of killer cells circulating vs. getting 8 hours of sleep. Take away most of the police and the bad guys can do what they want. Several epidemiological studies have

found that night time shift work that disrupts the circadian rhythm increases the risk of developing cancers including breast, prostate, endometrial, and colon.

A Danish study involving almost 25,000 people showed that getting 6 hours of sleep or less vs. getting 7 or more increased by 40% the odds of getting cancer. Another study looking at over 75,000 women over eleven years had similar findings.

One reason for increased risk of developing cancer is that reduced sleep stimulates the sympathetic nervous system, which provokes sustained inflammation. Cancer cells need their own blood supply to multiply out of control. Such cells have learned to hijack the inflammatory response and make a new blood supply to foster such growth. Cancer cells also use the inflammatory response to metastasize. Research done out of the U. of Chicago using sleep deprived mice found that there was a 200% increase in the speed and size of cancer growth compared to well slept mice.

Other studies have linked breast and prostate cancer to shift work because both are hormonally driven. It is thought that disruption of the circadian rhythm and melatonin is having an impact. Beyond regulating sleep, melatonin also is thought to suppress cancer growth. If you have inadequate melatonin such as from too much bright light, cancer rates go up. e.g. Research has found that people living in brighter lit neighborhoods have higher breast cancer rates. Breast cancer is the type that has been most studied relative to effects of light at night and shift work. A nationwide Danish study of 7,035 women with confirmed primary breast cancer found that at least a half year of predominantly working at night increased the risk of that cancer by 1.5 times. Other studies of night work have found breast cancer rates being increased up to three times over.

There are also higher rates of colorectal cancer from night shift work due to light exposure as found through the Nurses' Health Study. Another study found elevated rates of endometrial cancer from night shift work. Both of these findings are attributed to lower melatonin levels from working night shifts. The World Health Organization (WHO) has officially classified night time shift work as "a probable carcinogen."

### Sexual

For men, testosterone reaches its highest level while asleep, and need at least three hours of it to get to their peak blood level.

One experiment took healthy young men in their mid-twenties and limited them to five hours of sleep a night for a week. At the end of the week there was a marked drop in testosterone in their blood, equal to what being 10-15 years older would be like. Moreover, there was a 29% reduction in sperm count, and the sperm had more deformities. To top all this off such inadequate sleep also led to smaller testicles. Sleep apnea especially lowers testosterone levels too.

Beyond being a blow to the male ego, such facts have consequences. Low T brings on more tiredness and fatigue. Testosterone helps males maintain a sharper focus, and with less concentration is off. Sexual interest and ability naturally suffers with lower testosterone levels. Bone density is reduced, along with muscles naturally.

The good news about sex at least for men is that sexual activity and orgasm helps males fall asleep. Part of being able to reach an orgasm involves being able to relax, and that by itself may

promote sleep. Ejaculation also causes a release of chemicals impacting the brain, including noradrenaline, serotonin, oxytocin, vasopressin, nitric oxide, and the hormone prolactin, and it is this last one in particular that may help induce sleepiness. Oxytocin may help reduce stress levels too.

Women have problems stemming from reduced sleep too. Follicular releasing hormone that is needed for ovulation is reduced by 20% with sleep limited to 6 hours a night. A meta-analysis of 100,000 women found that irregular night time hours resulting in poor quality sleep, such as found with nurses who worked such shifts, had a 33% higher rate of abnormal periods than those working days. Women with erratic hours were 80% more likely to suffer from reduced fertility. Women who do become pregnant while sleeping less have a significantly higher risk of miscarriage in the first trimester vs. those getting 8 hours of sleep/night.

Hormonal fluctuations in women and their impact on sleep during monthly periods, pregnancy and menopause are far too complex to go into any detail here. But a few ideas can be offered.

Estrogen helps sleep onset, reduce the number of times a woman awakens, and increases the amount of total sleep that is gotten. It is also involved with temperature regulation, with low levels of it obviously being involved with hot flashes. And it has an effect on cortisol which is a stimulating hormone. Lower levels of estrogen in menopause therefore create higher levels of cortisol which is one reason why sleep then becomes worse.

Progesterone at least when given IV is sedating, and also increases GABA, a neurotransmitter that some have called 'nature's Valium.' That is, it is a calming chemical.

Insomnia is also related to anxiety and depression, in both women and men, and there is a chicken or egg issue to them. That is, each can cause the other. But there are also some other clues that suggest that treating insomnia can improve mood.

In studies conducted over a long time, insomnia appears to come first. Waking up multiple times a night allows one's brain to kick in and start worrying about all manner of stuff, such as the day just passed, the day coming up, kids, work, past traumas, present conflicts, not getting good sleep such as from awakenings, and a myriad of other issues that can buzz around in one's mind. And anxiety then sets in. So in the case of menopause, the progression is that menopause causes sleep disruptions which causes anxiety and/or depression.

In men and women, the likelihood of becoming depressed in the presence of unremitting insomnia is 39.8:1 according to one study – but only 1.6:1 if insomnia resolved. This suggests that treating insomnia can prevent depression.

### DNA

One study took healthy young men and women and restricted them to six hours of sleep for a week. Their DNA was then examined, and 711 genes were found to be distorted compared to the same people getting 8½ hours of sleep for a week. What was changed? Some of the genes that got accelerated as to their biological activity were for chronic inflammation, cellular stress, and various impacts on cardiovascular health, including reducing HDL (good cholesterol). Those genes that suffered reduced activity included for maintaining stable metabolism and optimal immune system responses.

There is also something called telomeres. They are sort of the like the end of a shoelace where there is a cap to keep the lace from unraveling. Telomeres are at the end of DNA strands and serve the same sort of purpose. Each time a cell reproduces telomeres shorten, and when they become too short the cell stops dividing or dies. Lifestyle choices such as diet, and activities (e.g. smoking, obesity, lack of exercise) also affect telomere shortening. And accelerated telomere shortening may increase the pace at which a person ages such as through cardiovascular disease, diabetes, osteoporosis, and increased risk of cancer of the lung, bladder, renal cell, GI, head and neck. People getting less or worse quality sleep have more damaged telomeres based on a number of studies from around the world done on people in their forties to sixties, although causation has not been proven as of now.

Sleep that is out of sync with the clock, such as doing shift work or getting it after jet lag also has an impact. Research done in England found that pushing forward the sleep-wake cycle by a few hours each day for three hours disrupted a lot of genes such as for controlling metabolism, temperature regulation, cardiac health, and the immune system in young, healthy adults.

### The 3<sup>rd</sup> leading cause of death in the U.S

...are medical doctors, when all their errors be it surgical, medication mistakes or otherwise are added up. Medical residents typically work 80+ hours a week with shifts that can last 30 hours non-stop and that is week in and week out. This is an improvement from not too long ago where they were working 100-120 hours a week, and some did two 36 hour stretches a week without any guaranteed sleep. (The training program for residents was first created by a doctor at Johns Hopkins back in 1889 who happened to have been a cocaine addict and went for days without sleep while bingeing on the drug. Such a demanding and unhealthy work schedule has stuck ever since basically due to the old boys club of ‘I did it, so now it’s your turn.’)

Research has found that after a thirty hour shift without sleep residents make 460% more diagnostic mistakes in the ICU than when well rested. Interns and residents pulling all nighters make 36% more serious medical errors, five times as many diagnostic mistakes, and twice as many “attentional failures” such as falling asleep during surgery. Research also has shown that limiting residents to a maximum of 16 hour shifts with 8 hours rest before the next one reduced serious medical errors by more than 20%. Moreover, 20% of residents cause significant harm to a patient during their residency, and 5% will kill a patient, both of these being due to lack of sleep. Going under the knife of an attending surgeon who has not had 6 hours of sleep the night before increases the risk of a serious surgical error occurring by 170%. Remember this if you are having elective surgery. Ask one question in advance, and perhaps prevent a serious error impacting your well being.

### REM sleep deprivation

REM serves different functions for us. One is that it can help us solve problems and be creative, as noted earlier such as famous people becoming inspired through their dreams. Another is improving our mental and emotional health.

Sleep is the only time that the anxiety triggering hormone noradrenalin is absent from the brain. With this hormone turned off we can remember emotional aspects of our lives to store – or to forget them without being crippled emotionally as to re-experiencing all the feelings again.

An experiment was done in which some emotionally provocative images were shown to two groups of people. One saw the images in the morning and again in the evening. The other group saw them in the evening, got a night’s worth of sleep, and saw them again the next morning.

MRI scans were then made during the second exposure to the pictures. Those who slept during the night found them less emotionally disturbing the second time around. And the MRI scan showed a large and significant reduction in the reactivity of the amygdala, which is the emotional center of the brain. Plus, the prefrontal lobe put a further emotional brake on the second exposure for the group that got sleep. Those who saw the pictures without any sleep had just as strong a reaction if not greater the second time than they did the first.

The subjects' sleep also had been recorded, and it was found that it was time spent in dream sleep that made the difference for dampening the emotional response.

### PTSD

Subjective reports of sleep disturbance occur in 70-91% of individuals who have PTSD, as to falling or staying asleep. Nightmares are commonly found in such people, and rates of their occurrence vary with the severity of their exposure to physical aggression.

One of the problems found in PTSD patients as to their having poor sleep is that they are an exception to the rule just stated above as to noradrenalin being absent during sleep. They have noradrenaline while sleeping which then blocks the ability to enter and maintain normal REM. What results is that the benefit of REM, namely working through the traumatic emotion by dreaming does not happen. A drug used for controlling blood pressure, Prazosin, happens to block noradrenaline. It was theorized that giving Prazosin to combat veterans would stop this noradrenaline issue from arising, and therefore better sleep would result. The VA has since gotten on the bandwagon and started prescribing the drug heavily.

The only problem is it does not work. A study called PACT that came out in 2018 looked at 304 vets across thirteen VA medical centers, comparing Prazosin to a placebo. There was no significant difference in the reduction of recurrent nightmares. Prazosin patients had higher rates of side effects such as for dizziness, light headedness and urinary incontinence. My own experience with thousands of vets I have seen who have been prescribed Prazosin is that zero have told me it has helped them.

There are other consequences for not getting enough REM sleep. One is being able to read subtle cues such as in facial expression, such as reflecting depression, frustration, anger or irritation. Research has been done and those that got a full night of sleep did well on such a task. The same people without adequate REM could not make such subtle distinctions. So what?

Think of occupations that tend to be sleep deprived such as those working long hours in the medical field (e.g. ER docs and nurses), law enforcement and military personnel, those handling emergencies, and new parents. Being able to accurately read facial expression can be a matter of life and death. A military guard who needs to identify 'friend or foe.' Police may only have a second to react as to whether or not to shoot someone. Without adequate REM sleep errors at such moments increase.

### Autism

People with autism spectrum disorder (ASD) often have abnormal sleep patterns. The circadian rhythm is weaker, with a flatter profile of melatonin across 24 hours, rather than a rapid rise at night and fall during the day. Day and night are less light and dark for them. Total amount of sleep in ASD kids is less too. Plus, there is a 30-50% deficit in REM sleep compared to non-ASD. There is now interest to see if there is causation here, but for now it is just a correlation.

But depriving an infant rat of REM sleep finds that they go on to become socially withdrawn and isolated as adolescents and adults.

What can be done to improve sleep?

### **Drink alcohol?**

Alcohol is the most common sleep aid, with at least 20% of Americans relying on it to help in falling asleep. How does it affect sleep? For one, it is one of the most powerful REM suppressors known. The metabolism of alcohol creates a by-product called aldehydes. And this chemical blocks the generation of REM sleep. An extreme version of REM deprivation can be found in alcoholics who go for long periods of time without dream sleep. The consequences are so large that their dreams burst through while awake and fully conscious, as to hallucinations and becoming grossly disoriented resulting in what are called the DT's (delirium tremens). If the person stops drinking such as in a rehab facility, there is a REM rebound, meaning that their real sleep is filled with REM for awhile.

The circadian rhythm that keeps us in a 24 hour cycle is disrupted by alcohol. Exposure to light, such as from the sun, helps keep our cycle in sync. Alcohol reduces the ability to respond to such light cues, and the effects on the circadian rhythm appear to persist even with no additional drinking.

Moreover, problems with the circadian rhythm from drinking can impact us by way of having a 'leaky gut' that allows bacteria, toxins, and food to leave the intestines and enter the blood, causing health consequences. Alcohol suppresses melatonin, and a moderate amount of booze an hour before bedtime can reduce the hormone by nearly 20%. Drinking also increases adenosine, creating more sleep pressure so that you may sleep at the wrong time and further throw off your natural sleep/wake cycle.

Still other issues: there is 'sleep' and there is 'sedation.' They are not the same. Alcohol causes the latter. Sedation can include building up a tolerance over time, meaning that you may need to increase the amount of drinking you do to knock yourself out at night. Drinking in the first half of the night also increases NREM and decreases REM sleep which can have an impact on our memory and emotional processing abilities. In the second half of the night the sedation of alcohol is dissipating. Sleep moves from deeper to lighter stages as a result, and there may be more awakenings even if only micro in nature which a person will not remember. But they still impact sleep quality. Alcohol may also increase REM here, and it is a lighter stage from which it is easier to awaken.

Then there is greater risk of snoring and sleep disordered breathing, such as from muscles in the neck and throat relaxing too much which can create apnea. Plus, drinking can contribute to next day tiredness, fatigue, irritability and problems concentrating. And there are hangovers.

One more problem to mention with alcohol is that it impairs learning and memory. One experiment had three groups of people learning something new, and it was the type of memory that REM sleep is known to promote. Everyone learned the new material to about 90% accuracy. One group got normal sleep for a week. A second group got a little drunk just before going to bed after they had learned the material that day. The third group learned the material and slept normally for two nights, and then got similarly drunk on the third night (sort of like 'partying

over the weekend'). All of the groups learned the material while sober, and were tested on day 7 while sober.

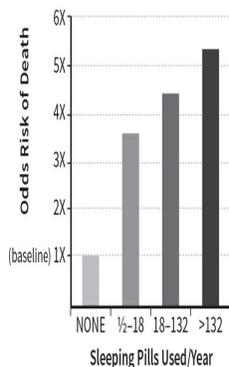
What were the results? The control group who slept normally remembered everything they had learned originally, and even showed some enhancement. The second group who got a little drunk the first night forgot over 50% of their original learning. The third group who were sober for the first two nights lost 40% of their original learning. This is **sleep rule #2 again**. That is, the learning process that occurs in sleep is not necessarily completed in a single night and thinking you can go into sleep quality debt, and pay it back on a following night is mistaken.

### Take sleeping pills?



First off, do sleeping pills work? Recently there was an analysis of all the research done on the newer sleep drugs (e.g. Ambien, Lunesta) involving almost 4,500 people. People in the studies subjectively felt they fell asleep faster and slept more soundly with fewer awakenings. Sleep recordings showed otherwise. In actuality, there was no difference from placebos being used. Both groups took the same amount of time to fall asleep and had the same soundness of sleep. This is the 'good news.'

What is the 'bad news'? Remember, sleep and sedation are not the same. Sleep solidifies memory, as discussed earlier. Research done on animals given Ambien found that it did not solidify memories but actually erased them by 50%.



Research out of UC San Diego found that people using sleep meds have a significantly higher risk of developing cancer, and dying over the years that various studies were conducted vs. those who did not take such meds. In 2012 over 10,000 people were compared with most taking Ambien (Zolpidem), and some using Restoril (Temazepam). They were contrasted to 20,000 well matched controls with similar age, race, gender and background who did not use sleeping pills. They also controlled for BMI, exercise history, smoking, and drinking, and looked at the rate of disease and death over 2½ years. As can be seen in the graph people taking more than 132 sleeping pills/year were 5.3 times more likely to die over the study period. Those taking just 18 pills/year were 3.6 times more likely to die. Similar results have been found from around the world in other studies.

Why we sleep, Matthew Walker

What were the people dying from? Infection for one. Recall how sleep boosts immune response. Sedation through such meds does not provide the same immune system boost.

Another killer is a higher rate of car accidents. Almost all people I see professionally who take such meds complain of being 'groggy' or 'hung over' in the morning from using such pills. Drive in that state and accident rates go up.

There is also a higher rate of stroke and heart disease from use of sleeping pills. Plus there is more of a risk for falls when using sleep meds, which is especially problematic for older individuals, such as from breaking a bone like their hip. Hip fractures in the elderly lead to a 20% mortality rate within a year. And, there was a 30% increased risk of developing cancer over the course of the 2½ years of the study for those taking high doses of Ambien, and 60% more

risk for those using just mild to moderate doses of Restoril. For now at least such research on cancer and sleep meds is not showing causation.

Another approach many use is to take a melatonin supplement. It is the fourth most popular natural product taken in the U.S. by adults, and second most popular given to kids. Melatonin is said to be unique in its antioxidant properties, in that its secondary, tertiary and quaternary metabolites also have antioxidant capabilities so even in low concentrations it can make a difference. Melatonin has other effects beyond impacting sleep. It protects mitochondrial and nuclear DNA meaning it helps prevent damage to it. Damaged DNA is basically another name for cancer. Fix the DNA in time and the cancer is avoided. Melatonin also raises glutathione levels which is a very important chemical with various functions including nourishing the immune system and removing toxins.

However, there are problems with taking a melatonin supplement. In my own experience with adults I have seen in my office, some number very close to 100% tell me that either a) it doesn't help with sleep, or b) it leaves them "groggy" or "hung over" in the morning. A good portion of mothers tell me it does help with their child's sleep.

Melatonin supplements do have other problems. One is that your body like the 'Goldilocks' level of chemicals, not too much, not too little, but just right. When you take a supplement your body says 'Whoa! Way too much!' and wants to cut back its own production of the hormone. If you stop taking it over skipping a night or going off altogether, you then have too little in your system and your sleep will be even worse.

Another is that normal melatonin levels at night are 5-25 *micrograms*. Taking a small dose of synthetic melatonin such as 0.25 milligrams would be 10-50 times greater than what is normal. Studies have shown that taking a 10 mg dose does not produce better results than 0.25 mg. And it is important to keep in mind that melatonin is a hormone and as such impacts many different parts of your body. Side effects of synthetic melatonin can include abnormal heart rhythm, elevated blood pressure, confusion, concentration difficulties, fatigue, dizziness, irritability, headaches, mood changes, depression, hypothermia, itching, seizures, sleep walking, vivid dreams, and reduced sperm count & motility. Moreover, it affects women's hormones such as estradiol, progesterone, luteinizing hormone, prolactin, cortisol, and thyroid. In the process it can disrupt ovulation with an obvious impact on the ability to conceive. It can also lower sex drive, and cause gynecomastia (breasts) in males.

Supplements are also not well regulated, and so what they actually contain as to dosage and impurities is not that well known. e.g. One study published in the Journal of Clinical Sleep Medicine in 2017 found poor quality in melatonin supplements. Thirty-one supplements were bought, and the actual dosage of the hormone varied from -83% to +458% of what was labeled, and 70% had concentrations that were 10% or less of what was claimed. The content of melatonin between lots of the same product varied by as much as 465%.

Other research published in The Medical Letter on Drugs and Therapeutics in 1995 found that four of six melatonin products from health food stores had unidentified impurities. Other problems include that it might worsen depression, increase blood sugar in diabetics, raise blood pressure in people who are taking certain drugs for hypertension, and increase the risk of seizures. It can also interact with birth control pills, blood clotting drugs, immune system suppressants, sedatives, and cardiac drugs.

Its safety in kids is not well known at this time. Animal research on it suggests that it could have an impact on reproductive, cardiovascular, immune and metabolic systems. It should not be used while breast feeding, and is not advised in pregnancy, those with autoimmune diseases, liver or kidney disease, epilepsy, stroke, people taking other meds, or consuming alcohol.

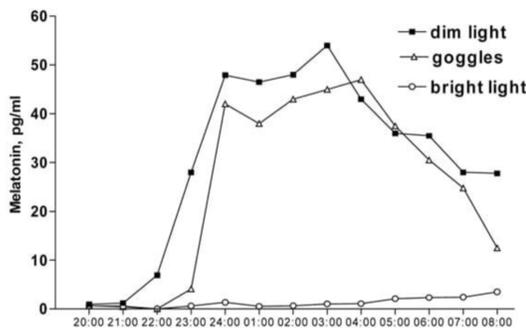
Having said all that, melatonin has its importance. What can reduce blood levels? Drugs that impact it include NSAIDs (e.g. Advil, Aleve), beta-blockers for high blood pressure (such as Atenolol, Metoprolol), birth control pills, hormone replacement therapy, loop diuretics, Hydralazine, and Theophylline. Foods that are naturally high in melatonin are said to include sour cherry juice concentrate in particular, sour cherries, pistachios, walnuts, corn, ginger root, rice, and peanuts to name a few. If you want a more thorough list look at <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5409706/>

A safer approach is to let your body make the right amount of melatonin for you. Dimming household lights a few hours before bedtime can help foster natural melatonin release in your body. Artificial light in the home can push back your circadian rhythm by 2-3 hours, so that it feels like you have sleep onset insomnia when you lie down. How dim? Less is more. Some research has found that 200 lux suppresses melatonin in adults. This level of light is what you may find in a public corridor, lobby or stairwell. A 60 watt incandescent puts out about 150 lux. Kids are even more sensitive to melatonin suppression from lighting at night and some research for 9-15 year olds found 1 hour of 15 lux at night to be detrimental. Experiment and see what works for you.

Avoiding use of smart phones, tablets, and other electronic screens for at least two hours before bedtime is advised as discussed earlier in this paper. If you want to use such electronic gadgets toward bedtime, or have a lot of blue light bulbs in your home, wear 'blue blocker' sunglasses or clip-ons that help avoid that color light from turning off your melatonin release at night. Research by the U. of Toronto looked at people inside wearing blue blocker glasses vs. those without them but were just in regular dim light. Melatonin levels were about the same.



The graph below shows what happened to a typical subject's melatonin levels...



“Blocking low-wavelength light prevents nocturnal melatonin suppression,” Leonid Kayumov et al

This graph shows results of a study done on nineteen men and women with an average age of about 25. ‘Bright light’ spectrum below 530 nm was blocked entirely by glasses. Women were on the pill, and matched for day of their menstrual cycle to avoid confounding effects on alertness, cognition, and melatonin levels. Dim light was defined as below 5 lux, bright light as 800 lux.

The findings included light between 470-525 nm having the biggest melatonin suppressing effects. Other findings included that blocking the shorter wavelengths did not impact attention span, concentration, or response accuracy. i.e. Shift workers could still do their job and not interfere with melatonin levels, while maintaining quality work and not being sleepy, or lacking in alertness.

What else works for improving sleep?

**Table 2.**  
Recommendations for the use of bright light to adjust body clock after time zone transitions.

	Bad Local Times (h) for Exposure to Light	Good Local Times (h) for Exposure to Light
<i>Time zones to the west (h)</i>		
3	0200 to 0800 <sup>a</sup>	1800 to 0000 <sup>b</sup>
4	0100 to 0700 <sup>a</sup>	1700 to 2300 <sup>b</sup>
5	0000 to 0600 <sup>a</sup>	1600 to 2200 <sup>b</sup>
6	2300 to 0500 <sup>a</sup>	1500 to 2100 <sup>b</sup>
7	2200 to 0400 <sup>a</sup>	1400 to 2000 <sup>b</sup>
8	2100 to 0300 <sup>a</sup>	1300 to 1900 <sup>b</sup>
9	2000 to 0200 <sup>a</sup>	1200 to 1800 <sup>b</sup>
10	1900 to 0100 <sup>a</sup>	1100 to 1700 <sup>b</sup>
11	1800 to 0000 <sup>a</sup>	1000 to 1600 <sup>b</sup>
12	1700 to 2300 <sup>a</sup>	0900 to 1500 <sup>b</sup>
13	1600 to 2200 <sup>a</sup>	0800 to 1400 <sup>b</sup>
14	1500 to 2100 <sup>a</sup>	0700 to 1300 <sup>b</sup>
<i>Time zones to the east (h)</i>		
3	0000 to 0600 <sup>b</sup>	0800 to 1400 <sup>a</sup>
4	0100 to 0700 <sup>b</sup>	0900 to 1500 <sup>a</sup>
5	0200 to 0800 <sup>b</sup>	1000 to 1600 <sup>a</sup>
6	0300 to 0900 <sup>b</sup>	1100 to 1700 <sup>a</sup>
7	0400 to 1000 <sup>b</sup>	1200 to 1800 <sup>a</sup>
8	0500 to 1100 <sup>b</sup>	1300 to 1900 <sup>a</sup>
9	0600 to 1200 <sup>b</sup>	1400 to 2000 <sup>a</sup>
10	Can be treated as 14 h to the west <sup>c</sup>	
11	Can be treated as 13 h to the west <sup>c</sup>	
12	Can be treated as 12 h to the west <sup>c</sup>	

For people with jet lag, a behavioral approach is to seek bright light, or avoid exposure (or at least wear dark sunglasses) for certain hours of the day, depending on how many time zones you have crossed travelling east or west.

a: promotion of a phase advance of the body clock

b: promotion of a phase delay of the body clock

c: body clock adjusts to large delays more readily than to large advances.

<https://www.youtube.com/watch?v=2q1ln6vaSE0&feature=youtu.be>

Shift work causing sleep problems can be approached through several means. This can include:

- ❖ if you work rotating shifts, ask your supervisor to change them clockwise, so that you start later than your prior shift, because it is easier to stay up late than go to bed early.
- ❖ try taking a nap or break before starting a night shift.
- ❖ review the drowsy driving statistics and car accidents of this paper, and realize that believing ‘I’m fine, I can drive safely’ may be the last mistake you make. Consider Uber, bus, a friend, or taking a nap before driving home.
- ❖ try to maintain the same sleep schedule on days you work and are off.
- ❖ if you can, try to ease into a long term change of schedule a few days in advance. For instance:

If you are currently working 5 PM – 1 AM, and sleeping from 3 AM – 11 AM, then a transition schedule might be something like:

1<sup>st</sup> night of transition sleep 5 AM -1 PM

2<sup>nd</sup> night of transition sleep 7 AM - 3 PM

3<sup>rd</sup> night of transition sleep 8 AM – 4 PM

New shift of 11 PM – 7 AM, sleep 9 AM – 5 PM.

Women can have problems sleeping during their periods for a number of reasons, such as cramps, bloating, and heavy bleeding. Body temperature also rises after ovulation. Try taking a warm bath or shower before bed, which can help dilate your blood vessels and cool you off some, which as noted earlier is beneficial for sleep. Moods change with the hormonal fluctuation, and different approaches to deal with them, such as through yoga, meditation, deep breathing, or a journal may help. Use a hot water bottle in bed to help with cramps, pain or bloating. Do exercise to improve your mood and improve sleep too.

For menopause, the best herbal approach with research behind it is black cohosh, such as helping somewhat with hot flashes. Soy has mixed results. Other herbs that have not been found to be effective include red clover, dong quai, and vitamin E. Given how poorly hormone replacement therapy has been found to be as to increasing risk of dying, such an approach will not even be discussed here.

For women in general, there are other approaches to consider to increase estrogen and progesterone. One is diet. Phytoestrogens (plant based estrogen) mimics natural and synthetic forms but are weaker in effect, with some research suggesting they have 1/400<sup>th</sup> – 1/1000<sup>th</sup> the potency of natural estrogen. This also means that they can carry some degree of risk, and all the

research is not yet in on this subject. Sticking to whole natural foods vs. isolated parts that have been concentrated by technology (e.g. processed soy products) may be a safer bet overall.

Phytoestrogens can be found in foods such as:

- ❖ flax seeds, sesame seeds, sunflower seeds
- ❖ fruits such as apples, dates, cherries, cranberries, grapes, apricots, oranges, strawberries, peaches, pomegranates, and many dried ones (e.g. apricots, dates, prunes)
- ❖ vegetables like yams, carrots, kale, celery, potatoes, beets
- ❖ soy products (tofu, miso soup, soy yogurt, milk)
- ❖ dark rye bread, bran cereals
- ❖ legumes such as lentils, peas, and pinto beans
- ❖ olives and olive oil
- ❖ chickpeas (garbanzo beans), mung beans, sprouts
- ❖ turmeric, thyme, sage, anise seed, sage, baker's yeast,
- ❖ beverages, such hops (as in beer), coffee, bourbon, red wine

If you would like an even broader list of foods with phytoestrogens, go to <https://www.superfoodly.com/estrogen-foods-list-50-high-phytoestrogen-sources/> and scroll down toward the bottom.

Progesterone may be boosted through foods such as:

- ❖ poultry
- ❖ red meat
- ❖ shellfish
- ❖ egg and dairy
- ❖ yams, sweet potatoes
- ❖ soy milk, fortified cereals, walnuts, whole grains

Another way to boost female sex hormones is to relax. Stress jacks up cortisol which lowers progesterone and estrogen.

Research out of U. of Texas, Austin suggested that testosterone levels in men can be raised by eating foods such as:

- ❖ olive, canola or peanut oil
- ❖ avocados
- ❖ olives
- ❖ almonds, cashews
- ❖ oysters
- ❖ wheat germ
- ❖ lobster and crab
- ❖ chickpeas (garbanzo beans), kidney beans
- ❖ oatmeal
- ❖ raisins
- ❖ dark green leafy vegetables
- ❖ bananas
- ❖ low fat yogurt

There are also two different approaches to improving sleep using cognition. CBT-I (cognitive behavioral therapy for insomnia) is one of them. How we think to a large extent affects how we feel. Many people have all manner of worries that impair sleep onset. Or, they awaken during the middle of the night from such worries and then can not fall asleep again. Such worries are over the day just passed, or next day stuff. Or worries over money, children, or work in general. Or, over traumatic events that have occurred in their life such as from experiencing combat in war, or being raped. There are ways to quiet the mind of such worries. CBT-I is now considered the best approach to use. In 2016 the American College of Physicians made an historic recommendation. After researching the issue they said that CBT-I must be used **as the first line treatment for all people with chronic insomnia, and not sleeping pills.**

There are certain types of ‘cognitive mistakes’ that individuals make that can impair sleep. For instance:

Cognitive error	Negative Thought	Positive Thought
<b>Unrealistic Expectations</b>	I should be able to sleep well every night like everyone else does.	Lots of people struggle with sleep from time to time. I’ll be able to do so with practice.
<b>Exaggeration</b>	Every night is another sleepless misery.	Some nights I do better than others.
<b>Catastrophizing</b>	If I don’t get some sleep, I’ll bomb out at work and lose my job.	I can get through work even if I’m tired. I can rest and relax tonight even if I don’t sleep well.
<b>Hopelessness</b>	I’ll never be able sleep. There’s nothing I can do about it.	My sleep issue can improve. If I focus on positive steps, I can sleep better.
<b>Fortune telling</b>	I know it’s going to take me an hour or two to fall asleep.	Maybe I’ll fall asleep quickly tonight if I use these strategies I’ve learned.

The ‘b’ of CBT-I means there are behavioral approaches you can use to improve sleep. These include:

- ❖ sleep restriction. This involves eliminating naps, and forcing yourself to stay up beyond your normal bedtime, which obviously makes you more tired. It can help build a stronger association between bed and sleep vs. bed and lying awake.
- ❖ limited purposes. Beds are meant for sex and sleep, and not working, watching tv, or anything else. It also means that you stay out of bed except for sleeping at your bedtime hours.
- ❖ improving your sleep environment. This means making your bedroom cool, quiet, comfortable, and dark. You can use a ‘white noise’ machine if need be, or ear plugs, or a blackout curtains, or a sleep mask. It also is best to avoid caffeine and nicotine later in the day. Regular day time exercise is also encouraged.
- ❖ relaxation techniques can include progressive muscle relaxation, meditation, guided imagery, and breathing exercises.
- ❖ biofeedback uses sensors that measure physiological measures such as heart rate, breathing, and muscle tension which can help you recognize and control them as a reflection of anxiety that can impact your sleep patterns.

Breathing exercises to help relax can include getting comfortable, closing your eyes, and inhaling through your nose and exhaling through your mouth, doing it slowly and deeply, and focusing on it.

Progressive muscle relaxation involves tensing major muscle groups progressively, one at a time (feet, legs, arms, etc.) for a count of ten, and then relaxing them, and after moving on to the next group.

There are numerous guided imagery mp.3 files you can find on the internet, such as <http://www.ilmpsychtesting.com/01MountainLake.mp3>

There are also any number of sleep apps that exist. The VA has created one designed especially for vets who have PTSD and impaired sleep. It is CBT-i Coach and is free. If you do not like it look around for another that better suits you.

Another cognitive approach is called image rehearsal therapy (IRT). It involves PTSD patients working with a therapist to in effect re-write their dreams, such as to content, themes, and endings. They then practice the rewritten script for 10-20 minutes a day, and monitor how well it works in subsequent dreaming at night. Results have shown it to be quite helpful.

Another approach for improving sleep or reducing impairment is the use of light. Not only is it good to avoid blue light at night, but red light can be helpful. Use of sunset-like colors prior to bedtime can help trigger natural melatonin production. There is lots on the net about this, such as <https://www.nestmaven.com/sleep/how-to-sleep-better/>

You can try using a sleep mask to eliminate any ambient light from sources such as clocks, and/or use ear plugs or white noise machines or apps to mask noises you can not control such as city traffic or the like.

Exercise is also good. Exercise has been found to increase total sleep time especially deeper NREM. Sleep onset is quicker, and fewer awakenings during the night occur with exercise too. Such findings have accrued to younger through older individuals. REM sleep is increased. It also can help lower stress hormones several hours after exercise is completed. As to how long to exercise, some say 20-30 minutes, others 30-45 minutes of moderate intensity being done at least several hours before dinner. Exercise revs up the body, and will make it harder to fall asleep. You want to unwind and relax prior to laying down in bed.

Mindfulness meditation can also be helpful. A study offered in JAMA Internal Medicine in 2015 took 49 middle and older aged people who had sleep problems. Half completed a mindfulness program teaching meditation and the other half received a sleep hygiene class. Both groups met six times, for a two hour class once a week. The meditation group ended up with less insomnia, fatigue and depression by the end of the sessions. The basic premise of this mindfulness is to choose a calming focus (e.g. focusing on your breathing, or repeating the word 'om' etc.). And then, let go and relax, and keep yourself focused on that matter, and not worry about other thoughts that intrude.

Like yoga? A study published in 2005 had 69 older people divided into three groups. One was yoga, another took an Ayurveda herbal preparation, and the third was a control group which got nothing ('wait listed'). The yoga group did significantly better, such as falling asleep faster by

ten minutes, total sleep per night increased by an hour on average, and they felt more rested in the morning.

Another approach to consider is acupressure. There has been some research using an elastic wrist band with a plastic button embedded in it, to be placed over an acupressure point. It can be found between the two tendons on the inside of the wrist, roughly three finger widths from the crease where the hand and wrist meet. The research showing it to be effective had the serious limitation of it not being a single much less double blind study.

Neurofeedback (EEG biofeedback) is another approach to improving sleep. Biofeedback has been studied for over fifty years, and it is helpful for improving various health issues. The concept is simple, and can be easily explained through the example of someone with high blood pressure looking at their reading on a blood pressure cuff, and then being told ‘Now, relax.’ What that means for each person is different, be it deep breathing, or thinking happy thoughts, or something else. But, the blood pressure reading can and will go down given some time and practice simply through getting the feedback from the cuff. The same principle applies to how your brain works. But instead of a blood pressure cuff an EEG machine is used in neurofeedback. It employs electrical leads gently attached to the scalp to only record your brain waves. No electricity is being put into your brain. Audio-visual feedback is determined by computer settings made by the therapist. The feedback allows you to change your brain’s functioning, such as reducing anxiety.

There are two different approaches to using neurofeedback. One is to work directly on sleep itself. And there is some research to show that it helps.

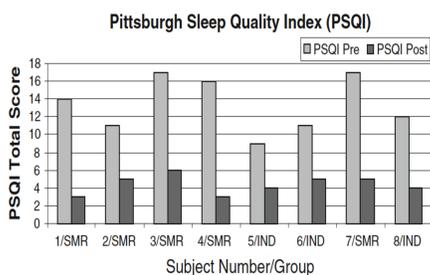


Fig. 2 PSQI pre-post change in global scores

One study with 8 participants had insomnia dating back anywhere from one year to starting in their childhood. They were given 15 training neurofeedback sessions, with 2 groups, sensory motor, SMR, & a more individual approach, IND. Various test measures were administered at the beginning and end of the treatment, including one of overall sleep difficulty that is considered “the most widely used, well researched, psychometrically sound instrument used in sleep research.” Scores above 5 are considered to reflect sleep impairment.

(“Neurofeedback for insomnia: A pilot study of z-score SMR and individualized protocols” [graphs above and below])

The total amount of sleep time was also measured, and there was an average of getting a little more than an hour extra per night. (There was one exception of a person who was later diagnosed with a severe medical problem that interfered with her sleep). The improvement in sleep was sustained for at least 6-9 months during follow-up in more than half of the people.

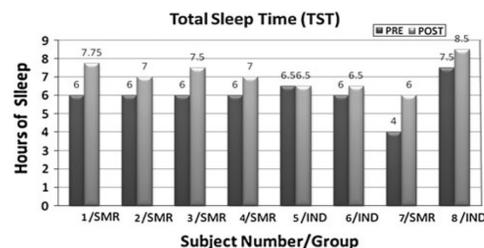


Fig. 4 Pre-post change in TST

Another approach to using neurofeedback to improve sleep is to reduce the factors that are impinging on it, such as anxiety, depression, PTSD, frustration, and irritability. Sleep is a fragile

commodity, and everyone has experienced nights where it is hard to fall and/or stay asleep because of worries or other stressors on one's mind.

One study was done by the USMC at Camp Pendleton involving 350 Marines who had PTSD and some also had TBI. They were given 10-40 sessions of neurofeedback and measured on over sixty symptoms as to pre- and post-treatment.

Symptom	% of people who had a decrease in symptoms (comparison of 'before' and 'after' treatment)
Suicidal thoughts	75%
Flashbacks	70%
Panic attacks	80%
Agitation	70%
Anxiety and depression	70%
Fears/phobias	60%
Night sweats	80%
Headaches	75%

About a quarter of the participants responded within 10-20 sessions. About half of them needed 20-40 sessions to get substantial improvement.

The most common complaints related to sleep difficulties, which involved 200 of the Marines. Psychological research measures the impact of treatment effectiveness in categories of 'small,' 'medium,' and 'large.' Neurofeedback's impact on the sleep of the Marines was rated as 'large.' Other 'large' impacts were on irritability, lack of motivation, and depression. Migraines were affected to a medium degree.

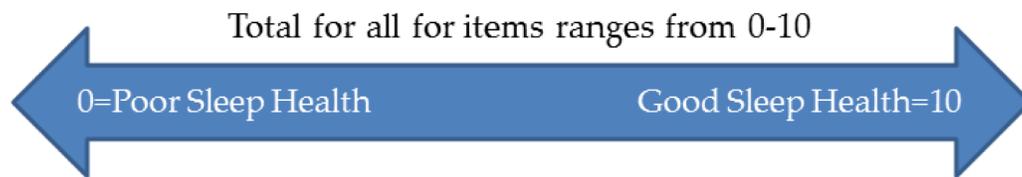
A final approach to mention for improving sleep is use of a weighted blanket. They have been tried to treat various groups of people such as autistics, depressed, and anxious, along with those simply having sleep difficulties. Quality research is generally lacking. There was one study done on autistics that used a randomized, controlled trial involving seventy-three kids ranging in age from about 5-17 years old, who were given a weighted or normal blanket and used a cross over design, so that each person had both types of blankets, with each for a two week period. The results were that the weighted blanket did not help autism spectrum kids sleep for longer periods of time per night, fall asleep significantly faster, or wake less often. The weighted blankets were liked by parents and kids, and were well tolerated.

In summary, NOW you have some education about sleep that you have been missing for all your life. You have choices to make as to working to improve the sleep you get and the benefits that accrue from it, or not. Just remember:

***“When you have your health, you have everything. When you do not have your health, nothing else matters at all.” -- Augusten Burroughs***

One quick and simple way to assess how well you sleep is offered below:

		Rarely/ Never (0)	Sometimes (1)	Usually/ Always (2)
<u>S</u> atisfaction	Are you satisfied with your sleep?			
<u>A</u> lertness	Do you stay awake all day without dozing?			
<u>T</u> iming	Are you asleep (or trying to sleep) between 2:00 a.m. and 4:00 a.m.?			
<u>E</u> fficiency	Do you spend less than 30 minutes awake at night? (This includes the time it takes to fall asleep and awakenings from sleep.)			
<u>D</u> uration	Do you sleep between 6 and 8 hours per day?			



[www.ncbi.nlm.nih.gov/pmc/articles/PMC3902880/bin/aasm.37.1.9s1.tif](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3902880/bin/aasm.37.1.9s1.tif)

Basic sleep advice as offered by the National Institutes of Health

("Tips for getting a good night's sleep" NIH Medline Plus,

Summer 2012.[medlineplus.gov/magazine/issues/summer12/articles/summer12pg20.html](http://medlineplus.gov/magazine/issues/summer12/articles/summer12pg20.html)):

- ❖ **Stick to a sleep schedule.** Go to bed and wake up at the same time each day. As creatures of habit, people have a hard time adjusting to changes in sleep patterns. Sleeping later on weekends won't fully make up for a lack of sleep during the week and will make it harder to wake up early on Monday morning.
- ❖ **Exercise is great, but not too late in the day.** Try to exercise at least 30 minutes on most days but not later than 2—3 hours before your bedtime.
- ❖ **Avoid caffeine and nicotine.** Coffee, colas, certain teas, and chocolate contain the stimulant caffeine, and its effects can take as long as 8 hours to wear off fully. Therefore, a cup of coffee in the late afternoon can make it hard for you to fall asleep at night. Nicotine is also a stimulant, often causing smokers to sleep only very lightly. In addition, smokers often wake up too early in the morning because of nicotine withdrawal.
- ❖ **Avoid alcoholic drinks before bed.** Having a "nightcap" or alcoholic beverage before sleep may help you relax, but heavy use robs you of deep sleep and REM sleep, keeping you in the lighter stages of sleep. Heavy alcohol ingestion also may contribute to

impairment in breathing at night. You also tend to wake up in the middle of the night when the effects of the alcohol have worn off.

- ❖ **Avoid large meals and beverages late at night.** A light snack is okay, but a large meal can cause indigestion that interferes with sleep. Drinking too many fluids at night can cause frequent awakenings to urinate.
- ❖ **If possible, avoid medicines that delay or disrupt your sleep.** Some commonly prescribed heart, blood pressure, or asthma medications, as well as some over-the-counter and herbal remedies for coughs, colds, or allergies, can disrupt sleep patterns. If you have trouble sleeping, talk to your healthcare provider or pharmacist to see whether any drugs you're taking might be contributing to your insomnia and ask whether they can be taken at other times during the day or early in the evening.
- ❖ **Don't take naps after 3 p.m.** Naps can help make up for lost sleep, but late afternoon naps can make it harder to fall asleep at night.
- ❖ **Relax before bed.** Don't overschedule your day so that no time is left for unwinding. A relaxing activity, such as reading or listening to music, should be part of your bedtime ritual.
- ❖ **Take a hot bath before bed.** The drop in body temperature after getting out of the bath may help you feel sleepy, and the bath can help you relax and slow down so you're more ready to sleep.
- ❖ **Have a good sleeping environment.** Get rid of anything in your bedroom that might distract you from sleep, such as noises, bright lights, an uncomfortable bed, or warm temperatures. You sleep better if the temperature in the room is kept on the cool side. A TV, cell phone, or computer in the bedroom can be a distraction and deprive you of needed sleep. Having a comfortable mattress and pillow can help promote a good night's sleep. Individuals who have insomnia often watch the clock. Turn the clock's face out of view so you don't worry about the time while trying to fall asleep.
- ❖ **Have the right sunlight exposure.** Daylight is key to regulating daily sleep patterns. Try to get outside in natural sunlight for at least 30 minutes each day. If possible, wake up with the sun or use very bright lights in the morning. Sleep experts recommend that, if you have problems falling asleep, you should get an hour of exposure to morning sunlight and turn down the lights before bedtime.
- ❖ **Don't lie in bed awake.** If you find yourself still awake after staying in bed for more than 20 minutes or if you are starting to feel anxious or worried, get up and do some relaxing activity until you feel sleepy. The anxiety of not being able to sleep can make it harder to fall asleep.
- ❖ **See a health professional if you continue to have trouble sleeping.** If you consistently find it difficult to fall or stay asleep and/or feel tired or not well rested during the day despite spending enough time in bed at night, you may have a sleep disorder. Your family healthcare provider or a sleep specialist should be able to help you, and it is important to rule out other health or emotional problems that may be disturbing your sleep.

Ok, so you now have received a semester's worth of education on sleep that you missed in your school years. **POP QUIZ!**

- 1) **True**  **False**  To be alert, awake and healthy during the day, all I need to do is drink sufficient caffeine.
- 2) **True**  **False**  To fall asleep at night and sleep well, all I have to do is take a pill or drink some alcohol.
- 3) Fill in the blank: I have come to appreciate the critical importance of sleeping well, and want to make improvements in how much and how well I sleep to safeguard my health and well being. Changes I plan and WILL make are:
  - a) \_\_\_\_\_
  - b) \_\_\_\_\_
  - c) \_\_\_\_\_
  - d) \_\_\_\_\_
  - e) \_\_\_\_\_
  - f) \_\_\_\_\_

Now, just do it!