



Sleep and Dreams

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Morpheus, the son of Sleep (ὕπνος), and the God of Dreams. The name signifies the fashioner or molder, because he shaped or formed the dreams which appeared to the sleeper. (*Ov. Met. xi. 635.*) He was the leader of the Oneiroi (Ονειροι), the personified spirits (δαίμων) of dreams. He was a messenger of the gods who appeared in the dreams of kings in human guise. Hence, one third of our life (sometimes more; at times, much less) we take refuge in the arms of a God –a minor one, but still...

Sleep and dreams have been puzzling humans forever. Intercessors (magi, priests, pythias, shamans, exorcists, fortune-tellers, psychics, and now neuroscientists) have offered *meanings* tailored to the events, the patsy, the zany of the day. We are still facing a big black box, or a series of Russian dolls-like mazes.

The major questions that immediately rise are: *What is Sleep?* and then *Why do we need Sleep?*



What Is Sleep?



Silence is the sleep that nourishes wisdom - Francis Bacon

The Wikipedia entry was revised and updated on 27 December 2017. It is long and comprehensive –as you can expect- but it brings, in lay language, a wealth of solid information:

Sleep is a naturally recurring state of mind and body, characterized by altered consciousness, relatively inhibited sensory activity, inhibition of nearly all voluntary muscles, and reduced interactions with surroundings. It is distinguished from wakefulness by a decreased ability to react to stimuli but is more easily reversed than the state of being comatose. Sleep occurs in repeating periods, in which the body alternates between two distinct modes known as non-REM and REM sleep.

Although REM stands for "*rapid eye movement*", this mode of sleep has many other aspects, including virtual paralysis of the body. A well-known feature of sleep is the *dream*, an experience typically recounted in narrative form, which resembles waking life while in progress, but which usually can later be distinguished as fantasy.

During sleep, most of the body's systems are in an anabolic state, helping to restore the immune, nervous, skeletal, and muscular systems; these are vital processes that

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maintain mood, memory, and cognitive performance, and play a large role in the function of the endocrine and immune systems.

The internal circadian clock promotes sleep daily at night. The diverse purposes and mechanisms of sleep are the subject of substantial ongoing research. The advent of artificial light has substantially altered sleep timing in industrialized countries.

Michel Valentin Marcel **Jouvet** (16 November 1925 – 3 October 2017) was Professor at the Collège de France –a colleague and friend of my father Bernard- and a Professor of Experimental Medicine at the University of Lyon. He was the Director of the Research Unit INSERM U 52 (Molecular Onirology) and of the Associated Unit UA 1195 of the CNRS (States of Vigilance - Neurobiology).

He described the electroencephalogram signs of cerebral death in 1959, and in 1961 categorized sleep into two different states: telencephalic (slow wave) sleep and rhombencephalic sleep (paradoxical sleep, known as REM sleep in English-language writings on the subject).



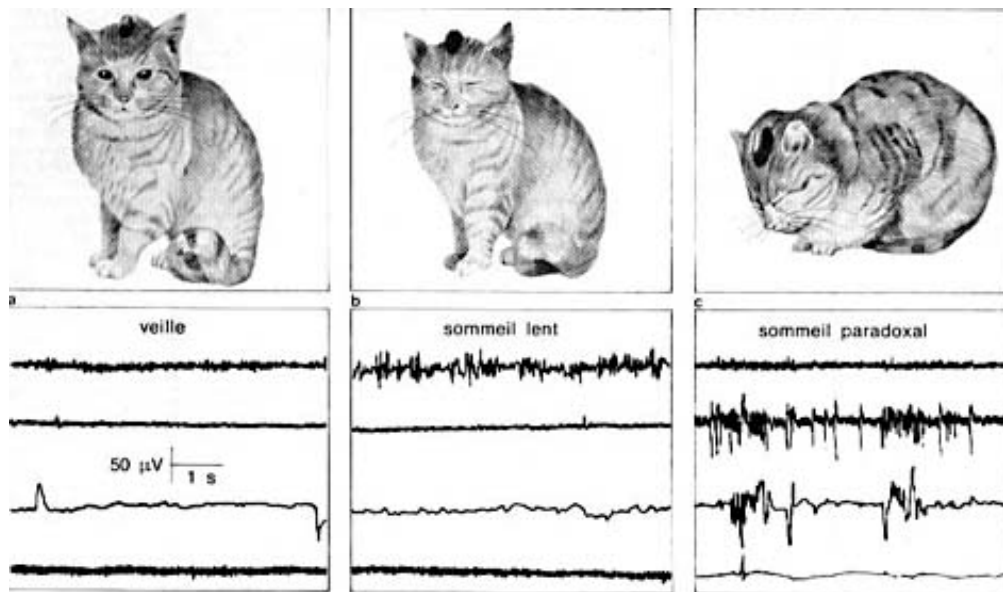
In *the Paradox of Sleep* (MIT Press, 1999) Jouvet proposed the speculative theory that **the purpose of dreaming** is a kind of iterative neurological programming that works to preserve an individual's psychological heredity, the basis of personality.

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He was elected in 1977 to the French Academy of Sciences; in 1991 he was awarded the prestigious *Prix mondial Cino Del Duca*. His works, and those of his team, have brought about the discovery of paradoxical sleep and to its individualization as the third state of functioning of the brain (1959), to the discovery of its phylogenesis, of its ontogenesis and its main mechanisms.

In 1959 Michel Jouvét conducted several experiments on cats regarding muscle atonia (paralysis) during REM sleep. Jouvét demonstrated that the generation of REM sleep depends on an intact pontine tegmentum and that REM atonia is due to an inhibition of motor centers in the *medulla oblongata*. Cats with lesions around the *locus coeruleus* have less restricted muscle movement during REM sleep, and show a variety of complex behaviors, including motor patterns suggesting that they are dreaming of attack, defense and exploration.



Michel Jouvét: Polygraphs of Cats dreaming

Jouvét was the researcher who first developed the analeptic drug Modafinil (Provigil®).

As mentioned above, the most pronounced physiological changes in sleep occur in the brain. Especially during non-REM sleep, the brain uses significantly less energy during sleep than it does in waking. In areas with reduced activity, the brain restores

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its supply of adenosine triphosphate (ATP), the molecule used for short-term storage and transport of energy. (Remember that in quiet waking the brain is responsible for 20% of the body's energy use; this reduction has a noticeable impact on overall energy consumption.)

Sleep increases the sensory threshold: sleeping persons perceive fewer stimuli. However, they can generally still respond to loud noises and other salient sensory events.

During slow-wave sleep, humans secrete bursts of growth hormone (children “grow” during sleep!). All sleep, even during the day, is associated with secretion of prolactin.

Measurements indicators of sleep include EEG of brain waves, electrooculography (EOG) of eye movements, electromyography (EMG) of skeletal muscle activity. Simultaneous collection of these measurements: polysomnography, can be performed in a sleep laboratory. Sleep researchers also use simplified electrocardiography (EKG) for cardiac activity and actigraphy for motor movements.

As Michel Jouvet demonstrated, sleep is divided into two broad types: non-rapid eye movement (non-REM or NREM sleep) and rapid eye movement (REM sleep); non-REM and REM sleep are so different that physiologists identify them as distinct behavioral states. Non-REM sleep occurs first and after a transitional period is called low wave sleep or *deep sleep*. During this phase, body temperature and heart rate fall, and the brain uses less energy. REM sleep (also known as *paradoxical sleep*), a smaller portion of total sleep time and the main occasion for *dreams* (or nightmares), is associated with desynchronized and fast brain waves, eye movements, loss of muscle tone, and suspension of homeostasis.

The sleep cycle of alternate NREM and REM sleep takes an average of 90 minutes, occurring 4–6 times in a good night's sleep.

The American Academy of Sleep Medicine (AASM) divides NREM into three stages: N1, N2, and N3, the last of which is also called delta sleep or slow-wave sleep. The whole period normally proceeds in the order: N1 → N2 → N3 → N2 → REM. REM sleep occurs as a person returns to stage 2 or 1 from a deep sleep. There is a greater amount of deep sleep (stage N3) earlier in the night, while the proportion of REM sleep increases in the two cycles just before natural awakening.

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Awakening can mean the end of sleep, or simply a moment to survey the environment and readjust body position before falling back asleep. Sleepers typically awaken soon after the end of a REM phase or sometimes in the middle of REM. Internal circadian indicators, along with successful reduction of homeostatic sleep need, typically bring about awakening and the end of the sleep episode. Awakening involves heightened electrical activation in the brain, beginning with the thalamus and spreading throughout the cortex.

During a night's sleep, a small portion is usually spent in a waking state. As measured by electroencephalography, young females are awake for 0–1% of the larger sleeping period; young males are awake for 0–2%. In adults, wakefulness increases, especially in later cycles. One study found 3% awake time in the first ninety-minute sleep cycle, 8% in the second, 10% in the third, 12% in the fourth, and 13–14% in the fifth. Most of this awake time occurred shortly after REM sleep.

Today, many humans wake up with an alarm clock. (Some people, however, can reliably wake themselves up at a specific time with no need for an alarm. Disclosure: I am one of these). Many sleep quite differently on workdays versus days off, a pattern which can lead to chronic circadian desynchronization. Many people regularly look at television and other screens before going to bed, a factor which may exacerbate this mass circadian disruption. Scientific studies on sleep have shown that sleep stage at awakening is an important factor in amplifying sleep inertia.

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Sleep timing is controlled by the circadian clock (Process C), sleep-wake homeostasis (Process S), and to some extent by individual will. - [For an in-depth exploration of the circadian rhythms, please read my essay *The Times of Time*, available on this website.]

The longer an organism is awake, the more it feels a need to sleep ("sleep debt"). This driver of sleep is referred to as Process S. The balance between sleeping and waking is regulated by a process called homeostasis.

Process S is driven by the depletion of glycogen and accumulation of adenosine in the forebrain that disinhibits the ventrolateral preoptic nucleus, allowing for inhibition of the ascending reticular activating system. Sleep deprivation tends to cause slower brain waves in the frontal cortex, shortened attention span, higher anxiety, impaired memory, and a grouchy mood. Conversely, a well-rested organism tends to have improved memory and mood. Neurophysiological and functional imaging studies have demonstrated that frontal regions of the brain are particularly responsive to homeostatic sleep pressure. Sleep debt does show some evidence of being cumulative. Subjectively, however, humans seem to reach maximum sleepiness after 30 hours of waking.

One neurochemical indicator of sleep debt is adenosine, a neurotransmitter that inhibits many of the bodily processes associated with wakefulness. Adenosine levels increase in the cortex and basal forebrain during prolonged wakefulness and decrease during the sleep-recovery period, potentially acting as a homeostatic regulator of sleep. Coffee and caffeine temporarily block the effect of adenosine, prolong sleep latency, and reduce total sleep time and quality.

A considerable amount of sleep-related behavior, such as when and how long a person needs to sleep, is regulated by genetics. Monozygotic (identical) but not dizygotic (fraternal) twins tend to have similar sleep habits. Neurotransmitters, molecules whose production can be traced to specific genes, are one genetic influence on sleep that can be analyzed. And the circadian clock has its own set of genes. Genes which influence sleep include ABCC9, DEC2, and variants near PAX 8 and VRK2. My own gene (see ref. UCSF) inherited from my father, allows me to wake up (very!) early wherever I am, and function decently well with 4-6 hours of sleep.

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The quality of sleep may be evaluated from an objective and a subjective point of view. Objective sleep quality refers to how difficult it is for a person to fall asleep and remain in a sleeping state, and how many times they wake up during a single night. Poor sleep quality disrupts the cycle of transition between the different stages of sleep. Subjective sleep quality in turn refers to a sense of being rested and regenerated after awaking from sleep. Homeostatic sleep propensity (the need for sleep as a function of the amount of time elapsed since the last adequate sleep episode) must be balanced against the circadian element for satisfactory sleep. Along with corresponding messages from the circadian clock, this tells the body it needs to sleep. A person who regularly awakens at an early hour will generally not be able to sleep much later than his/her normal waking time, even if moderately sleep-deprived. The timing is correct when the following two circadian markers occur after the middle of the sleep episode and before awakening: maximum concentration of the hormone melatonin, and minimum core body temperature.

Human sleep needs vary by age and amongst individuals, and sleep is adequate when there is no daytime sleepiness or dysfunction. Moreover, self-reported sleep duration is only moderately correlated with actual sleep time as measured by actigraphy, and those affected with sleep state misperception may typically report having slept only four hours despite having slept a full eight hours. Researchers have found that sleeping 6–7 hours each night correlates with longevity and cardiac health in humans, though many underlying factors may be involved in the causality behind this relationship.

Sleep difficulties are furthermore associated with psychiatric disorders such as depression, alcoholism, and bipolar disorder. Up to 90% of adults with depression were found to have sleep difficulties. Dysregulation found on EEG includes disturbances in sleep continuity, decreased delta sleep and altered REM patterns regarding latency, distribution across the night and density of eye movements.



We NEED Sleep!

The human organism *physically restores* itself *during sleep*, healing itself and removing waste which builds up during periods of activity. This restoration takes place mostly during slow-wave sleep, during which body temperature, heart rate, and brain oxygen consumption decrease.

The brain, especially, requires sleep for restoration, whereas in the rest of the body these processes can take place during quiescent waking. In both cases, the reduced rate of metabolism enables countervailing restorative processes. While awake, metabolism generates reactive oxygen species, which are damaging to cells. In sleep, metabolic rates decrease, and reactive oxygen species generation is reduced allowing restorative processes to take over.

The sleeping brain has been shown to remove metabolic waste products at a faster rate than during an awake state; sleep helps facilitate the synthesis of molecules that help repair and protect the brain from these harmful elements generated during waking. Anabolic hormones such as growth hormones are secreted preferentially during sleep. The concentration of the sugar compound glycogen in the brain increases during sleep and is depleted through metabolism during wakefulness. Wound healing has been shown to be affected by sleep.



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It has been shown that sleep deprivation affects the immune system: sleep loss impairs immune function and immune challenge alters sleep, and sleep increases white blood cell counts.

Sleep enhances memory, with procedural memory benefiting from late, REM-rich sleep, and explicit memory benefiting from early, slow wave-rich sleep.

During sleep, especially REM sleep, people tend to have ***dreams***: elusive first-person experiences, which, despite their frequently bizarre qualities, seem realistic while in progress. Dreams can seamlessly incorporate elements within a person's mind that would not normally go together. They can include apparent sensations of all types, especially vision and movement.

Sigmund Freud postulated that dreams are the symbolic expression of frustrated desires that have been relegated to the unconscious mind, and he used dream interpretation in the form of psychoanalysis in attempting to uncover these desires.

Counterintuitively, penile erections during sleep are not more frequent during sexual dreams than during other dreams. The parasympathetic nervous system experiences increased activity during REM sleep which may cause erection of the penis or clitoris. In males, 80% to 95% of REM sleep is normally accompanied by partial to full penile erection, while only about 12% of men's dreams contain sexual content.

Dreams are caused by the random firing of neurons in the cerebral cortex during the REM period; this explains the irrationality of the mind during REM periods, as the forebrain then creates a story to reconcile and make sense of the nonsensical sensory information presented to it. This also explains the odd nature of many dreams.

Using antidepressants, benzodiazepines (and derived sleep-inducers), acetaminophen, ibuprofen, or alcoholic beverages potentially suppresses dreams, whereas melatonin can encourage them.



Is Caffeine Bad –or even Good?

As mentioned above, caffeine interferes (interacts) with adenosine in the brain, but also in muscles (e.g. heart) -and almost everywhere in our body.

It's well-known that caffeine can, in extreme cases, be deadly. About 10 grams of the stuff will kill most people. But a typical cup of coffee has less than 100 milligrams—or just 0.1 gram—of caffeine. In other words, one would need to drink 100 cups of coffee in rapid succession to (possibly) hit the deadly dose. For people without underlying medical conditions, it's exceptionally hard to die from drinking caffeinated beverages because of how (relatively) little caffeine they contain.



This is something King Gustav III of Sweden found out in the 18th century, when he conducted an experiment to see whether tea or coffee kills faster. Both test subjects lived well into old age, far outliving King Gustav - and the researchers conducting the experiment.

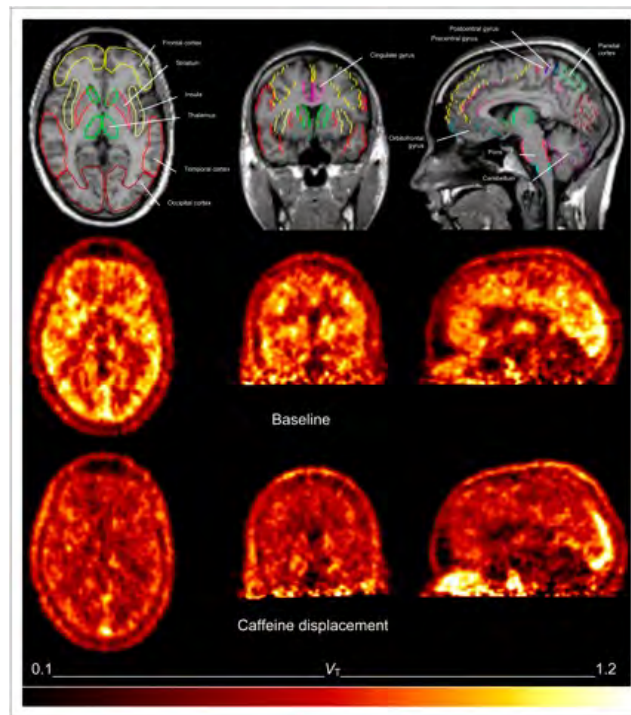
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There's little scientific evidence suggesting that even high amounts of caffeinated beverages can cause heart arrhythmias. A 2016 study found that patients at high risk for arrhythmias could imbibe 500 mg of caffeine in a five-hour span without raising their risk of irregular heartbeat.

Scientists and medical professionals concerned about caffeine generally focus on energy drinks, since they're wildly popular but contain lots of ingredients that interact in unknown ways, or on combinations of caffeine and alcohol, which get people drunker even as they continue to feel sober. But while energy drinks may be a relatively new concoction, coffee and tea and other traditional caffeinated beverages are not. And there's extensive research showing it's wrong to suggest typical caffeine consumption is dangerous.

When you drink a caffeinated beverage, the chemical immediately dissolves and spreads through all the fluids in your body. The caffeine crosses into the brain within minutes, where it latches onto proteins that normally receive adenosine, a chemical that makes you drowsy.



Caffeine blocks adenosine receptors in the brain

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Caffeine reaches its peak blood concentration between 45 and 60 minutes after you drink it. As time goes on, your liver degrades the caffeine in your blood, meaning there's less and less to elbow out the adenosine molecules that make you tired. So, before too long, you start to get sleepy again. In three to five hours, about half the caffeine from that cup of morning joe will have degraded; it might feel like time for a refill.

In addition, your brain receptors for adenosine are linked with receptors for dopamine, the “feel-good” chemical. Coffee makes you chipper not just because it's fighting off drowsiness; but also, because it makes it easier for dopamine to do its job, which in turn increases your feelings of pleasure. But dopamine is also the key ingredient to addiction; drugs like cocaine and amphetamine flood parts of the brain with it to hijack the brain's reward system—the mental circuitry of motivation. After getting flooded with those feelings of pleasure, you'll naturally seek those good feelings repeatedly. Motivation is important to keeping you alive, like when your brain is making you eat. But it's not so good when it's making you snort just one more line at 04:00 am when the bar is trying to close.

If you focus just on dopamine, caffeine looks sort of like very weak cocaine. It's clear caffeine has reinforcing effects; drinking coffee makes you want to drink more coffee. What isn't clear is whether it's truly addictive. It's a contentious topic. If “*caffeine-use disorder*” were to become a recognized diagnosis, it would appear alongside opioid-use disorder, tobacco-use disorder, and other often deadly addictions. This could “*minimize the severity of other substance-use disorders,*” says Maggie Sweeney, a psychiatry instructor at Johns Hopkins University. Others agree. “*It really trivializes other known addictions, such as smoking—we know those are clear addictions,*” says Marilyn Cornelis, an assistant professor at Northwestern University. “*If we were to ask someone to cut out smoking and they gave that up for a week, they might still crave it.... Coffee's a little different. You can think about someone cutting back on their coffee, and they could do it for a month. I don't think they're going to go crazy if they walk into a room with a bunch of coffee drinkers.*”

Addiction is typically understood to be the result of exposure to a substance that increases dopamine in brain structures. Caffeine makes the brain more sensitive to dopamine, but it doesn't increase levels of the chemical in the brain. In 2015, a US National Institutes of Health team undertook an experiment on humans and found

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no dopamine increase. For some scientists, this is clear evidence that caffeine is not addictive.

Astrid Nehlig, a research director at INSERM (French National Institute of Health and Medical Research), points out that addictions negatively impact people's lives, but caffeine generally does the opposite. *"You get dependent on caffeine, but why do you like caffeine?"* says Nehlig. *"Because it wakes you up, it increases your well-being, in addition to helping you be productive, etc. And it's also very often drunk in social conditions. You meet with people; you have a coffee. So, it's also part of a kind of ritual."*

Caffeine's short-term benefits are obvious. But studies show coffee does far more than help you focus and improve your mood. For example, lifelong coffee drinkers are less likely to have Alzheimer's, Huntington's, and Parkinson's diseases. In addition, if you consume caffeine in the morning, it can help maintain circadian rhythms, keeping your body's 24-hour internal clock consistent. When your circadian rhythms get out of whack, you're at risk for all sorts of sleep disorders, as well as weight gain and mental health issues. (Of course, caffeine's ability to affect your body's internal clock is also why it might be bad to consume caffeine at night.)

In fact, some researchers suggest we should be drinking three or four cups of coffee a day, if we want to reap the full benefits of caffeine without losing sleep or feeling agitated. That said, everyone handles caffeine differently; for some people four cups in a day might keep them up all night. This, it turns out, is coded into your genes. In the past few years, researchers have identified specific variations in the human genome that enable certain people to metabolize caffeine faster. That explains why everyone's experience with caffeine is different, and why any one-size-fits-all recommendation for caffeine is misguided. *"For someone who can't metabolize caffeine very quickly...one or two cups of coffee per day...might be equivalent to someone [else] drinking eight cups a day,"* says Cornelis. In a 2016 study, researchers discovered that people who drink the most coffee are also the people whose bodies have the genetic code to break caffeine down faster. In other words, the study sample population was already doing a good job self-regulating their intake. This suggests caffeine isn't dangerous for most people, since we naturally stick to our limits. So, when you get jittery or have trouble sleeping, you'll simply take that as a sign to drink a bit less in the future. And meanwhile, you'll be getting the daily benefits of caffeine, and perhaps even building up your body's defenses against neurodegenerative

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disease. In addition, it's very uncommon for people to have trouble cutting back on caffeine, if they do it gradually—say, foregoing that sixth cup of coffee, giving their body a week to re-equilibrate to five cups, then undergoing the same experience to get down to four cups a day and settling there. The one caveat is that this research applies to the way most adults consume caffeine—namely, drinking coffee to fight drowsiness or withdrawal-like symptoms.

Children often react very differently to the drug, likely due to several factors: their brains are still developing; they're consuming different types of caffeinated beverages; and they're drinking them for different reasons. Jennifer Temple, now director of the State University of New York-Buffalo's Nutrition and Health Research Laboratory, discovered that young people, ages 8-17, consume caffeine less consistently than adults, but more importantly, they consume it for entirely different reasons than adults: *"It's less about combating fatigue and more about things like, 'I use it to study for a test, or I use it to be better at playing video games, or I use it to feel high,'" Temple says. "They use a language that's much more about performance-enhancement or mood-elevation, whereas in adults, the language... is much more centered on withdrawal reversal- 'so I wake up in the morning, I don't want to get a headache, I don't want to feel sluggish, I'll drink my coffee.'" Temple says there's no evidence that small-to-moderate doses of caffeine are dangerous for 8-17-year-olds, but she generally recommends children avoid caffeine entirely, because they don't need it to be functional day-to-day, and it can interfere with their sleep.*

But millions –maybe billions- of people consume coffee daily, can afford it, enjoy it and find no significant adverse effect. Nor do scientists or health professionals.



Why do we NEED Sleep?

"To die, to sleep -
To sleep, perchance to dream - ay, there's the rub,
For in this sleep of death what dreams may come..."

William Shakespeare. Hamlet

The precise benefits of sleep are still mysterious, and for many biologists, the unknowns are transfixing. Even simple jellyfish must rest longer after being forced to stay up; there's a need to make up lost sleep, which has been seen not just in jellyfish and humans, but across the animal kingdom.

Why we feel the need for sleep is seen by many as key to understanding what it gives us. Biologists call this need "*sleep pressure*": stay up too late, build up sleep pressure. But like "*dark matter*," this is a name for something whose nature we do not yet understand. The more time we spend thinking about sleep pressure, the more it seems like a riddle game out of Tolkien: *What builds up over the course of wakefulness, and disperses during sleep? Is it a timer? A molecule that accrues every day and needs to be flushed away? What is this metaphorical tally of hours, locked in some chamber of the brain, waiting to be wiped clean every night?* In other words, "**What is the physical substrate of sleepiness?**"

Biological research into sleep pressure began more than a century ago. In some of the most famous experiments, Henri Piéron, a French scientist kept dogs awake for more than 10 days. Then, he siphoned fluid from the animals' brains, and injected it into the brains of normal, well-rested canines, which promptly fell asleep. There was something in the fluid, accumulating during sleep deprivation, that made the dogs go under. The hunt was on for this ingredient, this *hypnotoxin*, as Piéron called it, would reveal why animals grow drowsy, as he wrote in *Le Problème Physiologique du Sommeil* (Masson Ed., Paris, 1912).

If you needed proof that sleep, with its peculiar many-staged structure and tendency to fill your mind with nonsense, isn't some passive, energy-saving state, consider that golden hamsters have been observed waking up from bouts of hibernation -to nap. Whatever they're getting from sleep, it's not available to them while they're

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hibernating. Even though they have slowed down nearly every process in their body, sleep pressure still builds up. “*What I want to know is, what about this brain activity is so important?*” says Kasper Vogt, one of the researchers gathered at the new International Institute for Integrative Sleep Medicine (IIS) at Tsukuba University, near Tokyo Narita airport, Japan. He gestures at his screen, showing data on the firing of neurons in sleeping mice. “*What is so important that you risk being eaten, not eating yourself, procreation ... you give all that up, **for this?***”



University of Tsukuba, Japan, IIS

The search for the Piéron’s hypnotoxin was not unsuccessful. There are a handful of substances clearly demonstrated to cause sleep -including as we discussed- a molecule called adenosine, which appears to build up in certain parts of the brains of waking rats, then drain away during slumber. Adenosine is particularly interesting because of the adenosine receptors that caffeine seems to work on. When caffeine binds to them, adenosine can’t bind to these structures, which contributes to coffee’s anti-drowsiness powers. But work on hypnotoxins has not fully explained how the body keeps track of sleep pressure. For instance, if adenosine puts us under when we transition from wakefulness to sleep, where does it come from? “*Nobody knows,*” remarks Michael Lazarus, a researcher at the Tsukuba Institute who studies

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adenosine. Some people say it's coming from neurons, some say it's another class of brain cells. But there isn't a consensus. At any rate, "*this isn't about storage,*" says Masashi Yanagisawa, the Institute director. In other words, these substances themselves don't seem to store information about sleep pressure. They are just a response to it.



Masashi Yanagisawa

Sleep-inducing substances may come from the process of making new connections between neurons. Chiara Cirelli and Giulio Tononi, sleep researchers at the University of Wisconsin, suggest that since making these connections, or synapses, is what our brains do when we are awake, maybe what they do during sleep is scale back the unimportant ones, removing the memories or images that don't fit with the others, or don't need to be used to make sense of the world. "*Sleep is a way of getting rid of the memories in a way that is good for the brain,*" Tononi speculates.

Another group has discovered a protein that enters little-used synapses to cause their destruction, and one of the times it can do this is when adenosine levels are high. Maybe sleep is when this cleanup happens. One group at the Tsukuba institute, led by Yu Hayashi, is destroying a select group of brain cells in mice, a procedure that can have surprising effects. Depriving mice specifically of REM sleep by shaking them

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awake repeatedly just as they're about to enter it (a bit like what happens to the parents of crying babies) causes serious REM sleep pressure, which mice must make up for in their next bout of slumber. But without this specific set of cells, mice can miss REM sleep without needing to sleep more later. Whether the mice get away totally unscathed is another question—the team is testing how REM sleep affects their performance on cognitive tests—but this experiment suggests that where dreaming sleep is concerned, these cells, or some circuit they are part of, may keep the records of sleep pressure.

Yanagisawa himself has always had a taste for epic projects, like screening thousands of proteins and cellular receptors to see what they do. In fact, one such project brought him into sleep science about 20 years ago. He and his collaborators, after discovering a neurotransmitter they named orexin, realized that the reason the mice without it kept collapsing all the time was that they were falling asleep. That neurotransmitter turned out to be missing in people with narcolepsy, who are incapable of making it, an insight that helped trigger an explosion of research into the condition's underpinnings. In fact, a group of chemists at the Institute at Tsukuba is collaborating with a drug company in an investigation of the potential of orexin mimics for treatment.

These days, Yanagisawa and his collaborators are working on a vast screening project aimed at identifying the genes related to sleep. Each mouse in the project, exposed to a substance that causes mutations and fitted with its own EEG sensors, curls up in a nest of wood chips and gives in to sleep pressure while machines record its brain waves. More than 8,000 mice so far have slumbered under observation.

When a mouse sleeps oddly -when it wakes up a lot, or sleeps too long- the researchers dig into its genome. If there is a mutation that might be the cause, they try to engineer mice that carry it, and then study why it is the mutation disrupts sleep. Many very accomplished researchers have been doing this for years in organisms like fruit flies, making great progress. But the benefit to doing it in mice, which are extremely expensive to maintain compared to flies, is that they can be hooked up to an EEG, just like a person.

A few years ago, the group discovered a mouse that just could not seem to get rid of its sleep pressure. Its EEGs suggested it lived a life of snoozy exhaustion, and mice that had been engineered to carry its mutation showed the same symptoms. *"This*

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mutant has more high-amplitude sleep waves than normal. It's always sleep-deprived," says Yanagisawa. The mutation was in a gene called SIK3. The longer the mutants stay awake, the more chemical tags the SIK3 protein accumulates. The researchers published their discovery of the SIK3 mutants, as well as another sleep mutant, in *Nature* in 2016. While it isn't exactly clear yet how SIK3 relates to sleepiness, the fact that tags build up on the enzyme, like grains of sand pouring to the bottom of an hourglass, has the researchers excited. "*We are convinced, for ourselves, that SIK3 is one of the central players,"* says Yanagisawa.

As researchers probe outward into the mysterious darkness of sleepiness, these discoveries shine ahead of them like flashlight beams, lighting the way. How they all connect, how they may come together into a bigger picture, is still unclear. The researchers hold out hope that clarity will come, maybe not next year or the next, but sometime, sooner than you might think. On an upper floor at the International Institute for Integrative Sleep, mice go about their business, waking and dreaming, in row after row of plastic bins. In their brains, as in all of ours, is locked a secret.



The End of Sleep?

In the April 10, 2013, of *Aeon Magazine*, the science-writer Jessa Gamble, author of *The Siesta and the Midnight Sun: How We Measure and Experience Time* (2011), penned a remarkable essay on **New, Emerging Technologies that could radically reduce our need to sleep**. This chapter is an edited version of the *Aeon* piece.

Work, friendships, exercise, parenting, eating, reading — there just aren't enough hours in the day. To live fully, many of us carve those extra hours out of our sleep time. Then we pay for it the next day. A thirst for life leads many to pine for a drastic reduction, if not elimination, of the human need for sleep. Little wonder: if there were a widespread disease that similarly deprived people of a third of their conscious lives, the search for a cure would be lavishly funded. It's the Holy Grail of sleep researchers, and they might be closing in.

As with most human behaviors, it's hard to tease out our biological need for sleep from the cultural practices that interpret it. The practice of sleeping for eight hours on a soft, raised platform, alone or in pairs, is atypical for humans. Many traditional societies sleep more sporadically, and social activity carries on throughout the night. Group members get up when something interesting is going on, and sometimes they fall asleep in the middle of a conversation as a polite way of exiting an argument. Sleeping is universal, but there is glorious diversity in the ways we accomplish it.

Different species also seem to vary widely in their sleeping behaviors. Herbivores sleep far less than carnivores -four hours for an elephant, compared with almost 20 hours for a lion- presumably because it takes them longer to feed themselves, and vigilance is selected for. As omnivores, humans fall between the two sleep orientations. Circadian rhythms, the body's master clock, allow us to anticipate daily environmental cycles and arrange our organ's functions along a timeline so that they do not interfere with one another. Our internal clock is based on a chemical oscillation, a feedback loop on the cellular level that takes 24 hours to complete and is overseen by a clump of brain cells behind our eyes (near the meeting point of our optic nerves). Even deep in a cave with no access to light or clocks, our bodies keep an internal schedule of almost exactly 24 hours. This isolated state is called 'free-running', and we know it's driven from within because our body clock runs just a bit

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slow. When there is no light to reset it, we wake up a few minutes later each day. It's a deeply engrained cycle found in every known multi-cellular organism, as inevitable as the rotation of the Earth — and the corresponding day-night cycles -that shaped it.

One of the most valuable outcomes of work on sleep deprivation is the emergence of clear individual differences -groups of people who reliably perform better after sleepless nights, as well as those who suffer disproportionately. The division is quite stark and seems based on a few gene variants that code for neurotransmitter receptors, opening the possibility that it will soon be possible to tailor stimulant variety and dosage to genetic type.

Around the turn of this millennium, the biological imperative to sleep for a third of every 24-hour period began to seem quaint and unnecessary. Just as the birth control pill had uncoupled sex from reproduction, designer stimulants seemed poised to remove us yet further from the archaic requirements of the animal kingdom.

The executive functions of the brain are particularly vulnerable to sleep deprivation, and people who are sleep-deprived are both more likely to take risks, and less likely to be able to make novel or imaginative decisions, or to plan a course of action. Designer stimulants such as modafinil [invented by Michel Jouvet] and armodafinil (marketed as Provigil® and Nuvigil®) bring these areas back online and are highly effective at countering the negative effects of sleep loss. Over the course of 60 hours awake, a 400mg dose of modafinil every eight hours reinstates rested performance levels in everything from stamina for boring tasks to originality for complex ones. It staves off the risk propensity that accompanies sleepiness and brings both declarative memory (facts or personal experiences) and non-declarative memory (learned skills or unconscious associations) back up to snuff.

It's impressive, but also roughly identical to the restorative effects of 20 mg of dextroamphetamine or 600 mg of caffeine (the equivalent of around six coffee cups). Though caffeine has a shorter half-life and must be taken every four hours or so, it enjoys the advantages of being ubiquitous and cheap.

For any college student who has pulled an all-nighter guzzling energy drinks to finish an essay, it should come as no surprise that designer stimulants enable extended, focused work. A more challenging test, for a person wired on amphetamines, would

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be to successfully navigate a phone call from his or her grandmother. It is very difficult to design a stimulant that offers focus without tunneling -that is, without losing the ability to relate well to one's wider environment and therefore make socially nuanced decisions. Irritability and impatience grate on team dynamics and social skills, but such nuances are usually missed in drug studies, where they are usually treated as unreliable self-reported data. These problems were largely ignored in the early enthusiasm for drug-based ways to reduce sleep.

They came to light in an ingenious experimental paradigm designed at the government agency Defence Research and Development Canada. In 1996, the defense psychologist Martin Taylor paired volunteers and gave each member of the duo a map. One of the two maps had a route marked on it and the task was for the individual who had the marked map to describe it accurately enough for their partner to reproduce it on their map. Meanwhile, the researchers listened in on the verbal dialogue. Control group volunteers often introduced a landmark on the map by a question such as: *'Do you see the park just west of the roundabout?'* Volunteers on the stimulant modafinil omitted these feedback requests, instead providing brusque, non-question instructions, such as: *'Exit West at the roundabout, then turn left at the park.'* Their dialogues were shorter and they produced less accurate maps than control volunteers. What is more, modafinil causes an overestimation of one's own performance: those individuals on modafinil not only performed worse, but were less likely to notice that they did.

One reason why stimulants have proved a disappointment in reducing sleep is that we still don't understand enough about why we sleep in the first place. More than a hundred years of sleep deprivation studies have confirmed the truism that sleep deprivation makes people sleepy. Slow reaction times, reduced information processing capacity, and failures of sustained attention are all part of sleepiness, but the most reliable indicator is shortened sleep latency, or the tendency to fall asleep faster when lying in a dark room. An exasperatingly recursive conclusion remains that sleep's primary function is to maintain our wakefulness during the day.

Since stimulants have failed to offer a biological substitute for sleep, the new watchword of sleep innovators is *'efficiency'*, which means in effect reducing the number of hours of sleep needed for full functionality. The Defense Advanced Research Projects Agency (DARPA) -the research arm of the US military- leads the

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way in squeezing a full night's sleep into fewer hours, by forcing sleep the moment head meets pillow, and by concentrating that sleep into only the most restorative stages. Soldiers on active duty need to function at their cognitive and physiological best, even when they are getting only a few hours' sleep in a 24-hour cycle.



Nancy Wesensten, a psychologist for the Center for Military Psychiatry and Neuroscience at the Walter Reed Army Institute of Research in Maryland, has a mission to find ways to sustain soldier operations for longer, fighting the effects of acute or chronic sleep deprivation. She has argued that individual's sleep should be regarded as an important resource, just like food or fuel. Working with the Marine corps, Wesensten is not trying to create a super warrior who can stay awake indefinitely. She does not even see herself trying to enhance performance, as she already considers her subjects the elite of the elite. Everyone must sleep eventually, but the theatre of war requires soldiers to stay awake and alert for long stretches at a time.

Whereas the US Army and Air Force have a long history of adopting stimulants —

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pioneering modafinil applications and dextroamphetamine use in 24-hour flights — the Marines generally will not accept any pharmacological intervention. Like Wesensten, Chris Berka, the co-founder of Advanced Brain Monitoring (ABM), one of DARPA's research partners, says that she is cautious about the usefulness of stimulants, *'Every so often, a new stimulant comes along, and it works well, and there's a lot of interest, and then you don't hear anything more about it, because it has its limitations.'*

Some failed Air Force missions have drawn attention to the dangers of amphetamine-induced paranoia. Less than a decade after a 1992 Air Force ban on amphetamines, *'go pills'* were quietly reintroduced to combat pilots for long sorties during the war in Afghanistan. On 17 April 2002, Major Harry Schmidt, who had trained as a top gun fighter pilot, was flying an F-16 fighter jet over Kandahar. Canadian soldiers below him were conducting an exercise, and controllers told Schmidt to hold his fire. Convinced he was under attack, the speed-addled pilot let loose and killed four Canadian soldiers. The friendly fire incident resulted in a court martial, but in the media, it was the drugs that were on trial.

With military personnel in mind, ABM has developed a mask called the *Somneo Sleep Trainer* that exploits one or two-hour windows for strategic naps in mobile sleeping environments. Screening out ambient noise and visual distractions, the mask carries a heating element around the eyes, based on the finding that facial warming helps send people to sleep. It also carries a blue light that gradually brightens as your set alarm time approaches, suppressing the sleep hormone melatonin for a less groggy awakening.

For Marines at Camp Pendleton near San Diego (California), four hours of sleep or less is one of the rigors of both basic and advanced training. As a character-building stressor, night after night of privation is a personal endurance test but, as Wesensten has argued, it runs counter to other goals of their training, such as learning how to handle guns safely, and then remembering that information in a month's time. Berka agrees. *'We demonstrated cumulative effects of chronic sleep deprivation, even prior to deployment, and it was having an impact on learning and memory,'* she explained, after ABM had brought brain-monitoring devices into the camp for 28 days of measurement. *'It was defeating the purpose of training for new skill sets, and command acknowledged this was important.'* It's not cheap to equip dozens of trainees with

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night goggles and train them to distinguish foes from friends — all the while paying out salaries.

Darkness and diet are ways of practicing '*sleep hygiene*', or a suite of behaviors to optimize a healthy slumber.

The Somneo mask is only one of many attempts to maintain clarity in the mind of a soldier. Another initiative involves dietary supplements. Omega-3 fatty acids, such as those found in marine oils, sustain performance over 48 hours without sleep -as well as boosting attention and learning- and Marines can expect to see more of the nutritional supplement making its way into rations. The question remains whether measures that block short-term sleep deprivation symptoms will also protect against its long-term effects. A scan of the literature warns us that years of sleep deficit will make us fat, sick and stupid. A growing list of ailments has been linked to circadian disturbance as a risk factor.

Both the Somneo mask and the supplements -in other words, darkness and diet- are ways of practicing '*sleep hygiene*', or a suite of behaviors to optimize a healthy slumber. These can bring the effect of a truncated night's rest up to the expected norm -eight hours of satisfying shut-eye. But proponents of human enhancement aren't satisfied with normal. Always pushing the boundaries, some techno-pioneers will go to radical lengths to shrug off the need for sleep altogether.

Among these new players is Fisher, the president of Fisher Wallace Laboratories of Madison Avenue in New York, who acquired the patent for a transcranial stimulation device from the brothers Saul and Bernard Liss, both electrical engineers from the Massachusetts Institute of Technology. He sees the body as a collection of materials, some more conductive and others more resistant to electricity. '*The need to pierce bone and skull means we need a higher carrier frequency, which is the 15,000 Hz frequency. That's combined with 500 Hz and 15 Hz,*' Fisher says. '*It took eight to 12 years to derive those values. The body is influenced by frequencies between zero and 40 Hz.*' Those searching for a treatment for insomnia are Fisher's biggest and fastest-growing market. Someone with intractable insomnia will try just about anything to get some sleep.

Transcranial direct-current stimulation (tDCS) is a promising technology in the field of sleep efficiency and cognitive enhancement. Alternating current administered to

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the dorsolateral prefrontal cortex through the thinnest part of the skull has beneficial effects almost as mysterious as electroconvulsive therapy (ECT), its amnesia-inducing ancestor.

Negative effects on the brain have not yet been observed, and the FDA has approved some devices, such as the Fisher Wallace Stimulator, for unsupervised home use, but long-term effects are still unknown. The neurologist Soroush Zoghi and his team at Harvard Medical School are on the trail of how, exactly, these clinical outcomes are achieved. Once this is established, potential dangers will be easier to look for.

Using a slightly different technique -transcranial magnetic stimulation (TMS), which directly causes neurons to fire- neuroscientists at Duke University could induce slow-wave oscillations, the once-per-second ripples of brain activity that we see in deep sleep. Targeting a central region at the top of the scalp, slow-frequency pulses reach the neural area where slow-wave sleep is generated, after which it propagates to the rest of the brain. Whereas the Somneo mask is designed to send its wearers into a light sleep faster, TMS devices might be able to launch us straight into deep sleep at the flip of a switch. Full control of our sleep cycles could maximize time spent in slow-wave sleep and REM, ensuring full physical and mental benefits while cutting sleep time in half. Your four hours of sleep could feel like someone else's eight. Imagine being able to read an extra book every week -the time adds up quickly.

The question is whether the strangeness of the idea will keep us from accepting it. If society rejects sleep curtailment, it won't be a biological issue; rather, the resistance will be cultural. The war against sleep is inextricably linked with debates over human enhancement, because an eight-hour consolidated sleep is the ultimate cognitive enhancer. Sleepiness and a lack of mental focus are indistinguishable, and many of the pharmaceutically based cognitive enhancers on the market work to combat both. If only it were possible for the restorative functions that happen during sleep to occur simply during waking hours instead... One reason why we need to shut down our conscious selves to perform routine maintenance is that our visual system is so greedy. Glucose metabolism is a zero-sum game, and functional MRI studies show a radically different pattern of glucose metabolism during sleep, with distinct regions activated either in active or sleep states but not in both. As soon as we close our eyes for sleep, a large proportion of available energy is freed up. Just as most planes must be grounded to refuel, we must be asleep to restore our brains for the next day. A

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radical sleep technology would permit the equivalent of aerial refueling, which extends the range of a single flight (or waking day).

Such attempts are likely to meet with powerful resistance from a culture that assumes that 'natural' is 'optimal'. Perceptions of what is within normal range dictate what sort of human performance enhancement is medically acceptable, above which ethics review boards get cagey. Never mind that these bell curves have shifted radically throughout history. Our contemporary sleep habits are not in any sense natural, and ancestral human sleeping patterns would be very difficult to integrate into modern life.

Human enhancement is now being driven by military imperatives, at least in the US, because civilian society is more conservative in its approach. Dedicated divisions such as the US Air Force's Human Effectiveness Directorate try to make humans better at what they do naturally. It's a missed opportunity for a society-wide push to understand and reduce our need to power the brain down for hours every day. Every hour we sleep is an hour we are not working, finding mates, or teaching our children; if sleep does not have a vital adaptive function to pay for its staggering opportunity cost, it could be *'the greatest mistake the evolutionary process ever made'*, in the words of Allan Rechtschaffen, the pioneering sleep researcher and professor of psychiatry at the University of Chicago.

As biologists map the details of the human genome, they are looking for genetic markers that code certain behaviors and tendencies. One gene they hope to locate is the *"sleep gene"* -if it exists. Certain genes, such as CLOCK BMAL1, are known to play an important role in the body's circadian rhythm. But another gene - DEC2- might be the secret to light sleeping. Mutations to DEC2 significantly reduce the amount of sleep time that's required for the human body. The military is, as expected, a major consumer for such genetic technology: SEALs and Green Berets could be able, after gene therapy, to soldier on for days at a time during operations. They would accomplish missions without drowsiness, disorientation and slower reflexes.

In her award-winning Beggars trilogy of the 1990s, the American science fiction writer Nancy Kress posited a world in which genetic modification has become *de rigueur*. One of these 'genemods' -cooked up by gifted children let loose in a lab-eliminates sleep and even bucks the sci-fi convention of dire side effects, instead endowing the fortunate Sleepless with bonuses of greater intelligence and emotional

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stability. The side effects are, instead, societal -the unevenly distributed technology becomes the basis of a social schism, in which a perpetually productive elite rules a sleep-dependent majority of Livers. Kress presciently anticipated the ethical implications of our emerging era of what the neuroscientist Roy Hamilton of the University of Pennsylvania has dubbed '*cosmetic neuroscience*', or the tailoring of our ancient brains to suit our modern demands.

Should technologies such as tDCS prove safe and become widely available, they would represent an alternate route to human longevity, extending our conscious lifespan by as much as 50 per cent. Many of us cherish the time we spend in bed, but we don't consciously experience most of our sleeping hours -if they were reduced without extra fatigue, we might scarcely notice a difference except for all those open, new hours in our night time existence. Lifespan statistics often adjust for time spent disabled by illness, but they rarely account for the ultimate debilitation: lack of consciousness. Now a life lived at 150 per cent might be within our grasp.

Are we brave enough to choose it?



The Future of Sleep

Futurists are accustomed to launching headfirst into some very complex subjects, but even the most high-minded and enthusiastic of prognosticators may take a pass when it comes to dealing with the future of sleep. It's just that we humans -those in the developed world at least- maintain such a complicated relationship with sleep. We are taught that we need it, seem to love it while we're engaged in it and spend our waking hours moaning to each other about how much more of it we desire. But then we do everything in our power to delay its natural onset each night.

Psychologists tell us that much of that struggle is classically existential; having to do with the subconscious realization that our time among the living is finite, so we attempt to make the most of the hours we're fully conscious. Much more of it, however, must do with the allure of technology that began with the introduction of artificial lighting about 100 years ago and continues to plague us. In fact, we are currently in the throes of a major downward spiral, as all manner of blinking and buzzing gadgets keep us working, worrying and watching.

"Sleep in a lot of ways is kind of like rebooting your computer, only it's an 8-hour process of rebooting your body," says Thomas Frey. *"But can we do that faster, quicker and more frequently in the future?"* In doing so humans are sidestepping a biologic imperative, sleeping less than ever before in history despite enjoying a longer lifespan than all previous generations that roamed the Earth. More than one third of us are not getting enough sleep, reports the CDC (Center for Disease Control), with most of us enjoying just six hours per night of such recuperative time.

But if technology is to blame for the current imbalance, might we also utilize it to usher in a corrective sleep-filled future?

Ian Peterson, a renowned physicist and futurist, thinks so. In a 2011 report, he envisioned a world where technology geared toward sleep would revolutionize our bedroom environment. Much of what Peterson imagined is on its way to being realized: "smart" pajamas, bed clothing and mattresses outfitted with sensors to measure brain-body data -especially our responses to pressure, light and

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temperature -that will then be fed to mechanical beds; thermostats and lighting fixtures which adjust themselves on the fly to create and maintain a highly personalized optimal sleep experience; but who will need these, or just buy any of them?

If all of that seems a bit farfetched, consider the *Fitbit* you're wearing now — the one that's invisibly tethered to a smartphone app that's already monitoring, recording and sharing your personal health data. Consider, too, the burgeoning "*smart home*" industry whose affordable and easily operated hardware and apps allow us to adjust the lighting, temperature and security features of our homes from anywhere in the world. And consider that somewhere around 2023 approximately one trillion hyperlinked sensors will have been implanted in our everyday surroundings. By 2036 the figure jumps to one hundred trillion...



All these data should be controlling something, so why not use them to study and improve sleep?

Why not, indeed, say futurists Jack Uldrich and Thomas Frey. Both men see the future of sleep as inexorably linked to big data and the supercomputers that will employ artificial intelligence to provide new insights on sleep that take us well beyond Peterson's safe and sensible environmental modifications. "*By then, the real*

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vanguard will be a question of how to use sleep to further education, figuring out how to get the rest we need while also using sleep as a really productive time.” The real future of sleep, it seems, is located just off the transhumanist highway.

Obtaining any kind of reliable roadmap for such a trip is the difficult part for now, particularly if you’re expecting either Uldrich or Frey to offer one up. As futurists who seem comfortably planted at the conservative end of their profession’s spectrum, they’re reluctant to pinpointing their ideas along any hypothetical timeline. One reason for this reluctance is that so many will take it for prophecy. Another is that *“there are just too many variables,”* says Frey. *“Computing that kind of exponential growth can mess with your head in lots of ways.”* Maybe we’ll become accustomed to taking *“braincations,”* ones where our dreams go beyond the wildest expectations of virtual reality enthusiasts.

Ultimately, the new sleep will come down to *“personalized optimization,”* meaning it will be customized to an individual’s specific biology and brain functioning and be utilized for more than just rest. Perhaps sleep will be used to heal emotional and physical wounds, to earn a diploma or even to learn a new language. *“We are already using brain scanning technology to get very fuzzy pictures of dreams,”* says Uldrich. *“So it will become a matter of how we use it to alter our sleep experience. In other words, are the Disney Pixar releases of the far future not meant for a movie screen but instead meant for our dreams? When does Dreamworks really become dream works?”*

Transhumanists are not alone in their desire to push the limits of what is natural. As mentioned above, big government agencies like DARPA want to create hyperawake soldiers and fighter pilots who no longer suffer the affliction of sleep. For those like transhumanist Zoltan Istvan, optimization is defined as nothing less than *“curing the disease”* of sleep. Such a radical notion is to be expected given that the whole point of transhumanism is to transcend humanity with the aid of technology -to unite man and machine, if necessary, in ways that push evolution to the next level as rapidly as possible. To transhumanists, and maybe even to our post Singularity progeny, the human requirement for sleep, the equivalent of roughly one third of a person’s lifetime, can only impede transformation.

Transhumanists are not alone in their desire to push the limits of what is natural. In fact, as you slumbered last night, an astounding number of research scientists and technicians in labs around the world were busy searching for a cure. And they’re

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getting better at it. The science may only be in its infancy but already there's the "go-pill" modafinil, that staves off the debilitating effects of sleep-related fatigue for a limited duration. Transcranial brain stimulation (TCBS) and implants are also in the works, as mentioned in a previous section. Both can operate with the swipe of a smartphone app, zapping you into a trance-like state that lasts just minutes but is incredibly refreshing. If test results are to be believed, the jolt is as productive and restful as an hours-long siesta. *"If we can speed up the brain to learn quicker, can we also speed it up to sleep faster? That's counterintuitive but slowing the brain down to sleep better may not be the right direction at all."*

A far smaller percentage of us -those with deep pockets and a sense of daring -will get to experience sleep optimization to the max. That frantic time in the future where we can begin routinely speeding the brain through its sleep cycle, taking FDA-approved pills as sleep workarounds, and even successfully genetically engineering humans who require less sleep may be a major tipping point. Ultimately, says Uldrich, *"Humanity may evolve into two different species: one that favors the slower, natural evolutionary process and another -the Kurzweilian branch -that will embrace an enhanced evolutionary process."*

To be clear, Uldrich assures us that *"much of Earth's population will continue to sleep very much the way it always has,"* probably even better. But the net result for the "sleep optimized," Uldrich and Frey agree, is that they will likely become more productive, energetic and creative, and this will undoubtedly provide them with a competitive advantage in life. *"The analogy I use to describe the split, though not a perfect one, is the Amish living amid the rest of the world,"* adds Uldrich. *"Roughly two centuries ago they essentially said to society, 'Look, you can continue to embrace technology. We don't judge you for it but we just don't like what it's doing to our families and communities, so we reject it. And we hope you'll just let us live in peace.' I think we will see very bright, intelligent people who will come to a difference of opinion on the matter. But I don't think there is a right or wrong answer."*

If there's a cautionary note to consider, it should do with the risk of unintended consequences. Or, as Frey puts it: *"Lots of things that can go wrong when you change some fundamental tenant of the human condition. Let's say we had some instant sleep device, but after ten years of using it people turned into psychopathic killers - well, you see where that's heading, right?"* *"For whatever reason, we humans evolved based on a*

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circadian rhythm, so maybe we should just respect the wisdom of evolution before we push it to its limits,” Uldrich concludes. “Having said that, however, pushing limits is just what evolution is. We conduct experiments to see if we can become more productive, creative, healthier and happier -and maybe even to offer a new human experience. But we must recognize that most of them are going to fail. We have to keep that in mind and simply say, “This is the way life plays out.”

That may be true, but maybe in 50 years we’ll be asking each other about when sleep became so complicated.



Sleep and the Light at the End of a Tunnel



The dreams and current (but not yet verifiable) predictions of futurists are exciting –just as the latest *Star Wars* movie. But if we want to look at progress and the realistic future of uncovering more among the mysteries of sleep, there is one place that is built on solid tradition, and delivers regular breakthroughs: Stanford University, in Northern California.

The Stanford Sleep Medicine Center, the first one in the USA when it opened, has played a critical role in the development of the field of sleep medicine.

The Center was founded by Dr. William C. Dement and Dr. Christian Guilleminault (my former colleague at the Salpêtrière in Paris in the late 1950s) in 1970 and has been the site of numerous advances in sleep ever since.

Today the Stanford Center for Sleep Sciences and Medicine is an internationally renowned sleep center recognized for outstanding patient care and innovative sleep medicine research. In 2009, the Stanford Sleep Medicine Center moved to a state-of-the-art facility in the new Stanford Medicine Outpatient Center in Redwood City

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(California). The sleep center has 14 clinical beds, four additional beds dedicated to research and treats more than 5,000 adults and children each year, including patients from all over the world.

The Stanford Sleep Medicine Center works to improve coordination among the various specialties involved in treating patients. Its faculty includes specialists in obstructive sleep apnea, insomnia, narcolepsy, pediatric sleep, parasomnias, restless legs syndrome, and other sleep disorders. The clinical staff is comprised of psychologists, psychiatrists, neurologists, pulmonary specialists, and pediatricians. In addition, all work closely with sleep apnea surgeons, dentists, and orthodontists, who specialize in the treatment of sleep disorders. The Center has more than 100 doctors, research faculty, staff, and students who are devoted to the study and treatment of sleep and sleep disorders.

As the birthplace of sleep medicine, the center has a long history of important contributions to the field of sleep medicine. The Sleep Center spans across multiple scientific and medical specialties. Research interests range from seeking the genes associated with sleep disorders to studying the neurological and chemical systems that regulate sleep and waking. It hosts several basic research labs ranging from genetics to neurobiology, as well as an active clinical research department with projects in areas such as insomnia, narcolepsy, obstructive sleep apnea, comparative effectiveness and disease registry.

The Sleep Center at Stanford's unmatched reputation is due to the visionary work, dedication, tireless energy, creativity and warm connection with all who approach him, of William C. Dement.

This short video is arguably a well-deserved homage:

<https://youtu.be/UWkeI45kbNU>



Acknowledgements

This essay is stuffed and padded with (too many) references. The major ones –that I plundered, often verbatim- are listed. I concluded by coming back home: we live on the Western edge of Stanford University campus, and I visit its Departments often; I beg for forgiveness.

Yves P. Huin, besides his devotion, friendship and webmaster's skills, has been an astute editor.

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