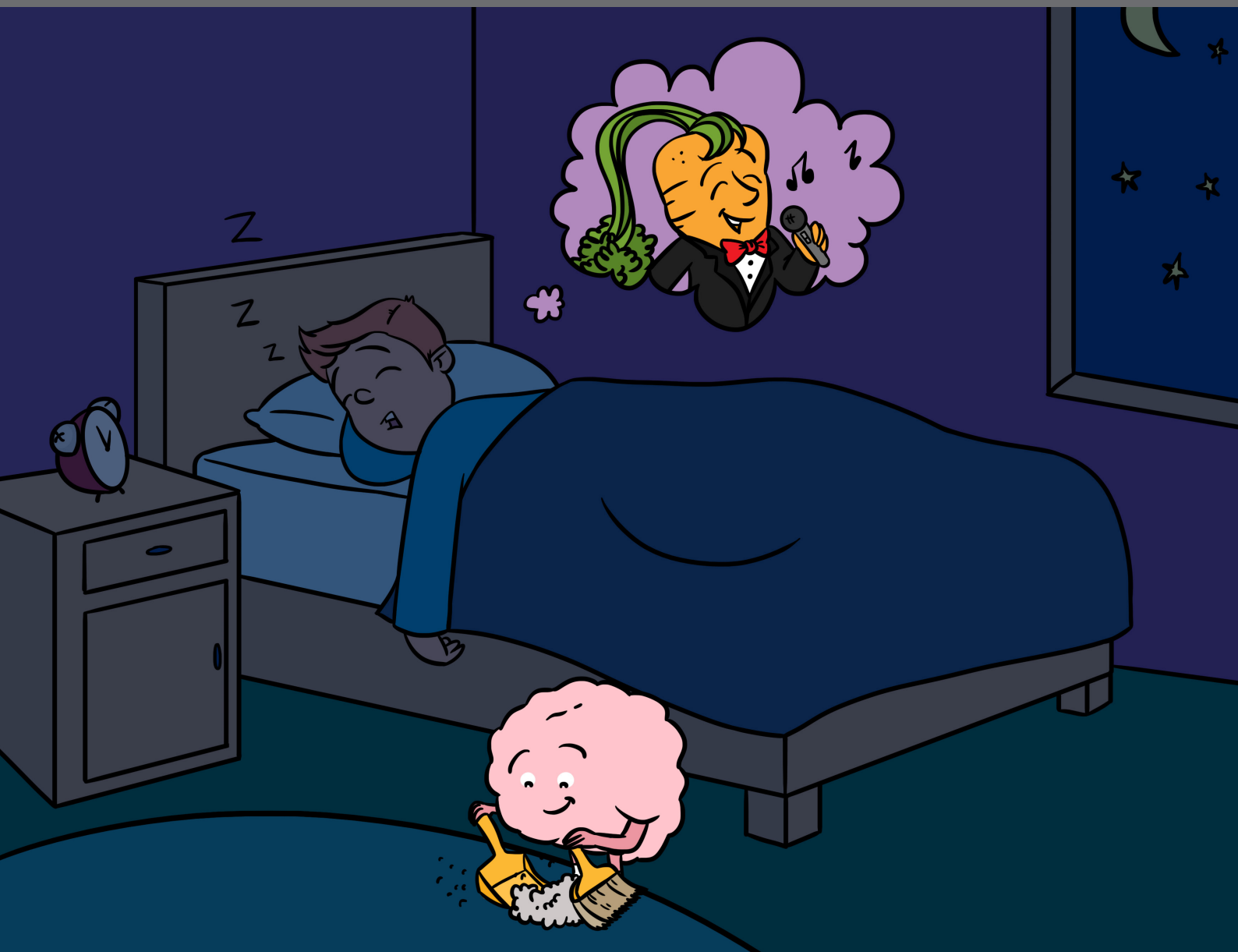


YOU SNOOZE, YOU DON'T LOSE - WHAT IS SLEEP AND WHY IS IT SO CRUCIAL?

EDITED BY: Frontiers for Young Minds
PUBLISHED IN: Frontiers for Young Minds





frontiers

FOR YOUNG MINDS

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ISSN 2296-6846

ISBN 978-2-83250-491-8

DOI 10.3389/978-2-83250-491-8

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YOU SNOOZE, YOU DON'T LOSE - WHAT IS SLEEP AND WHY IS IT SO CRUCIAL?

Topic Editor:

Frontiers for Young Minds

We spend an incredible amount of time sleeping – probably more time than we spend on doing anything else. This retrospective Collection of 8 articles takes a deep dive into sleep. Wow your brain and test your knowledge with this accessible overview of all things sleep(y).

The mystery of sleep has kept curious minds awake for millennia. From the times of the Greeks and Romans, people worshipped Gods associated with sleep: Hypnos (also Somnus) and his sons Morpheus, Phobetor and Phantasus – you might be able to see in these names the roots of familiar modern words associated with sleep and dreaming, such as “hypnosis”, “somnambulism” (sleepwalking), “morphine” (a sleep-inducing painkiller) and “fantasies”. Sleep is so important that famous names from William Shakespeare to the Beatles have written about it.

Over the centuries, scientists have begun to solve this mystery. We spend a third of our lives sleeping but not all sleep is the same. As we begin to drift to sleep, our body rests and recharges. However, our brains do not snooze as much. Neurons housekeep during this time: memory processing and finetuning cognitive functions rely on a good night's sleep. And all this while we dream. Dreams are a common experience: sometimes funny, scary, or downright bizarre, they are a fascinating combination of our inner and outer world! The information processing and self-organisation that the sleeping brain does in our dreaming state is so complex that, before it was well understood, it sparked famous theories such as the psycho-analyst Sigmund Freud's “Interpretation of Dreams”. Our sleeping brain makes us rest at night, while the quality of sleep energizes us for the day to come.

The first articles in this Collection focus on what makes a good night of sleep, and why it is essential for our well-being and health. Did you know that you actually continue learning while sleeping? A good night's sleep is like a symphony of brain rhythms with each movement serving a different function. Find out why you shouldn't cut it short, and how sleeping disorders sadly do just that.

As you discover the importance of sleep, the second set of articles will let you understand what is happening whilst sleeping. What do our brains do during this time? And how can we study the evolution of sleep? Some populations of Mexican cavefish may hold the answers.

Talking about non-humans: did you know that we are not the only creatures with a fascinating biological clock that is coordinated by the brain? The third set of articles leads us on an adventure back in time, and brings alive the series of experiments that

led to the discovery of the biological clock, today known as the circadian rhythm, and how modern life has cut the night short.

And lastly, we have two teaser articles: Have you been curious as to why we dream and how we can investigate dreams? Or have you ever wondered why some people sleep talk and whether this is similar to how we speak whilst awake? Find out in the last two articles of this Collection.

Our Collection will give you plenty of new ideas to dream about!”

Citation: Frontiers for Young Minds., ed. (2022). You Snooze, You DON'T Lose - What is Sleep and Why is it so Crucial? Lausanne: Frontiers Media SA.
doi: 10.3389/978-2-83250-491-8

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Why sleep?

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Reviewed by:



Eleanor
8 years old

We human beings spend about a third of our lives sleeping. That means that if you live to 90, you'll sleep for about 30 years – probably more time than you'll spend doing anything else. Sleep is really important since we cannot live without it and spend so much time doing it. Yet unlike the other basic biological drives such as eating and reproducing, we still don't understand exactly why we need to sleep. It used to be thought that sleep was mainly to rest and restore the body and the mind, and to keep us safe from predators that hunted at night. But over the last 15 years, this view has radically changed. We now know that sleep plays an essential role in learning, memory and emotional well-being. In this review, we'll first discuss the structure of a good night's sleep, and then the role of sleep in learning and memory.

A GOOD NIGHT'S SLEEP

Just as a good meal is made up of different kinds of food, a good night requires different kinds of sleep. A night of sleep can be divided into rapid eye movement (REM) and non-REM sleep, and non-REM sleep can be further broken down into four different stages based on the type of activity in the brain (See Figure 1). This activity can be measured using a technique called electroencephalography (EEG), which involves placing sensors on the scalp that detect the brain's electrical activity. During the night, you pass through the different stages, from lighter to deeper sleep and back again over and over again, every 90 minutes. In the wee hours of the morning, sleep becomes lighter and you spend more time in REM sleep, which means more dreaming.

In addition, the different patterns of brain activity seen in these sleep stages serve different functions, and as a result each stage helps with specific kinds of learning and memory.

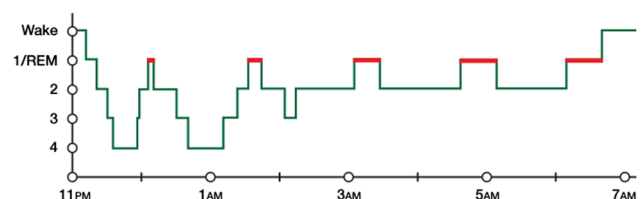


FIGURE 1 - A good night's sleep.

The normal progression of sleep stages across a night of uninterrupted sleep. REM sleep is highlighted in red. On the y-axis are wake, REM sleep, and the four sleep stages. On the x-axis is time. The green line shows how much time is spent in each sleep stage.

SLEEP, LEARNING AND MEMORY

Scientists once thought that all of our learning occurred during the day, while we are awake. Now we know that the brain continues to work on new information for days and even years, and that much of this continued learning happens while we're asleep. Sleep is involved in strengthening new memories and fitting them in with what we already know, and changing and updating our older memories based on what we just learned. But we do not remember everything we learn during the day. Somehow, the sleeping brain knows what new information is important enough to keep and what can be allowed to fade away [1]. Here are some examples of the many kinds of learning and memory that we need to sleep on.

PROCEDURAL LEARNING

Procedural learning means learning how to do something. When you're learning a new skill, like skiing or playing the piano, you may have the experience of reaching a point during practice where you just can't get any better. But when you try again the next day, right away your performance is much, much better. For most types of procedural learning, this improvement happens while you're asleep, and not just after some amount of time. For example, if you spend 10 minutes typing a sequence of keys on a computer keyboard over and over, as fast as you can, after the first 5 minutes you just don't get any faster. But the next morning you'll not only be faster, but you'll be typing more smoothly. On the other hand, if you train in the morning and test that evening with no sleep in between? Nada, zip, zero. You won't be any better [2]. Interestingly, not all sleep helps. The overnight improvement is greater if you spend more time in Stage 2 sleep (See Figure 1) and have more sleep spindles, which are brief, powerful bursts of brain activity that occur during Stage 2 sleep.

INSIGHT

Most everyone has heard of "sleeping on a problem," but does it really work? A group of German researchers taught students how to do a special kind of mathematical problem [3]. Unknown to the students,

there was a much easier way to do it, but almost none of them figured it out. Twelve hours later, they were tested again. Some students were trained in the morning and tested 12 hours later (with no napping) that evening, but they weren't much better. Only about 22% figured out the shortcut. In contrast, when students were trained in the evening, and tested 12 hours later after a good night of sleep, 60% of them – two and a half times as many – discovered the shortcut. So sleep can lead to insights!

EMOTION

It is common knowledge that you're likely to be more emotional after a poor night's sleep. So it is not surprising to find evidence that disrupting sleep makes it harder to manage your feelings. For example, after not getting enough sleep, people who are shown either pleasant or upsetting pictures have more activity in the amygdala, a part of the brain involved in emotions. In one study, the amygdala did not communicate as well with another part of the brain that normally helps to control emotional reactions, the prefrontal cortex (See Figure 2). Unfortunately, the

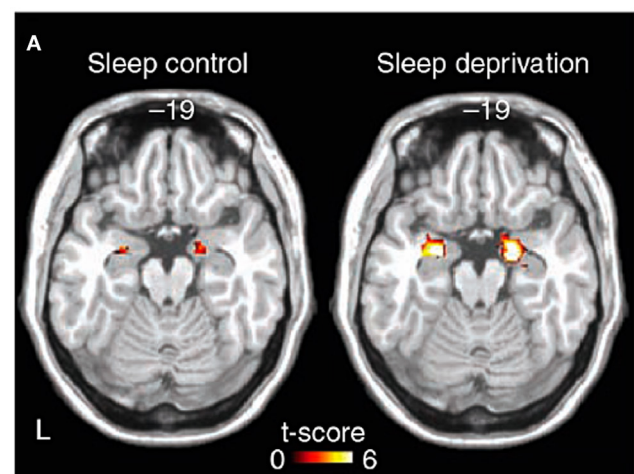


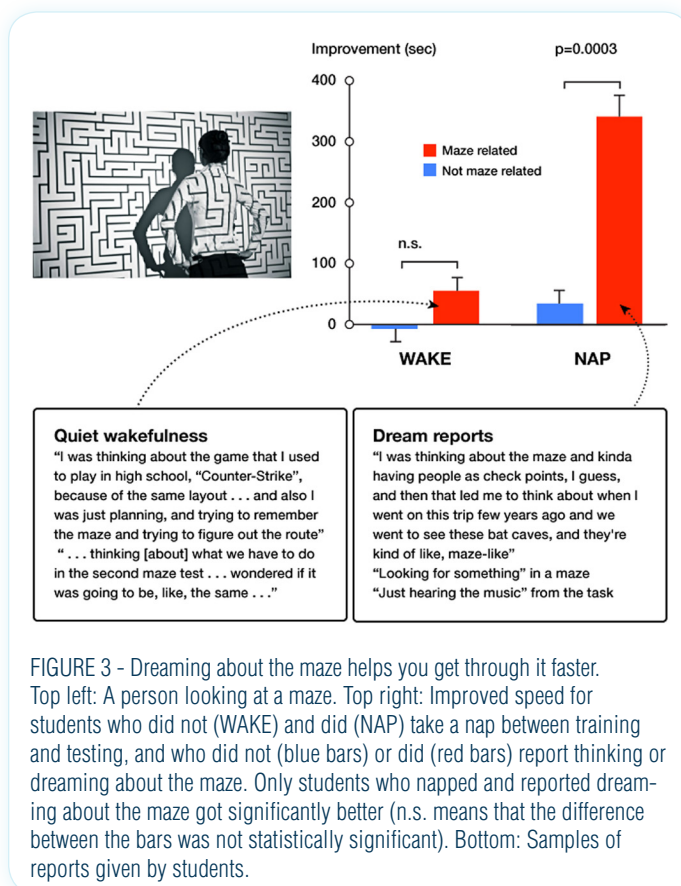
FIGURE 2 - The effects of not enough sleep on a part of the brain involved in emotion, the amygdala.

These horizontal MRI slices show structures deep in the brain. The colors show brain activity in the amygdala while research participants viewed unpleasant pictures compared to neutral pictures. Comparing the right to the left brain slice shows that participants who were deprived of a good night's sleep (right) had more activity in the amygdala than those who slept well (left).

sleeping brain remembers unpleasant memories better than neutral ones. While these memories may be more important to our survival, remembering mostly the bad things that happen can color your outlook and the decisions you make.

SOLVING MAZES DURING DREAMS

When students play an arcade style video game where they have to find their way through a complex maze, they can actually get better at it by simply taking a nap after practicing. Does dreaming have anything to do with this improvement in their memory of the layout of the maze? It's starting to look like the answer is, Yes. When researchers woke the students up during their naps and asked them what they had been dreaming about, it turned out that those who reported that they were dreaming about something related to the maze later showed ten times more improvement than those who didn't! (See Figure 3).



WHAT HAPPENS IF YOU DON'T SLEEP ENOUGH?

When you don't sleep enough, well, you become tired. And aside from the bad health effects of not enough sleep (people who don't sleep enough tend to eat more and unhealthier foods, gain weight, and get sick!), you also don't learn as well the next day and have trouble paying attention. It's almost as if your brain is too full to absorb any more information. For some information learned the day before, it's like you've missed the opportunity to press the 'save' button – it's gone forever. For other learning, you just don't show the normal sleep-dependent improvement (like for that piano piece you practiced). You are also more emotionally reactive to both pleasant and unpleasant events, which can lead you to feel stressed out, yell at friends and make bad decisions, based more on emotion than reason.

SO WHAT'S THE BOTTOM LINE?

Get enough sleep, and don't sleep with your cell phone by your side. Sleep is too important to miss. A good night's sleep is like a symphony of brain rhythms with each movement serving a different function. Cut it short, or let it be interrupted by a text or a tweet, and you may miss the chance to have a breakthrough on that thorny problem you were sleeping on, or to perfect that piano piece just in time for the recital. And it's not like you can make up for it the next night – you'll probably have to start from scratch. Keep in mind that most teenagers need at least 9 hours of sleep per night! So here's wishing you many good nights of sleep and sweet dreams.

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Submitted: 13 October 2013; Accepted: 30 October 2013; Published online: 13 November 2013.

Citation: Manoach, D. S., and Stickgold, R. (2013). Why sleep? Front. Young Minds. 1:3. doi: 10.3389/frym.2013.00003

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REVIEWED BY:



Eleanor, 8 years old

I like reading and drawing. My favorite colors are blue, silver, pink, and purple. My favorite food is creamed spinach. I like to go shopping with my Mom.

AUTHORS



Dara S. Manoach

She is a scientist who uses brain imaging tools to reveal how different parts of the human brain work together when we think, learn, and solve problems. This information helps us to understand and treat brain disorders in which thinking is disturbed such as schizophrenia and autism.



Robert Stickgold

He studies how sleep and dreaming make our memories stronger and last longer, while also trying to figure out what they really mean, and whether they are even worth keeping. His work suggests that sleeping is a big part of learning, and sometimes as important as studying!



THE SUPERPOWERS OF OUR SLEEP

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MARTINA
AGE: 8

Sleep is a fundamental function of the human body and it is crucial for our well-being and health. Most people are not aware of the importance of sleep. Only few adopt good sleep habits and sleep enough hours. This can lead to several consequences, such as problems with attention and memory and the development of diseases. Each one of us has an internal rhythm that changes as we develop. Respecting the number of hours of sleep needed by our bodies is crucial. The practice of good sleep habits can help us have a good night's sleep. However, some sleep problems can be more difficult to treat and a sleep specialist might be necessary to evaluate the situation and provide the appropriate treatment. Understanding

sleep and recognizing its importance will help you to sleep better and, ultimately, to have a healthy life.

Sleep is essential for our well-being and health. It is a natural and basic function important for all organisms, from microorganisms to plants to humans, independent of gender, ethnicity, age, or culture. Even many years ago, Greeks and Romans worshiped gods associated with sleep, like Hypnos and his Roman equivalent, Somnus. Poor sleep is for humans what Kryptonite is to Superman: it weakens us. It is not by chance that, on average, one third of our day is spent asleep.

CIRCADIAN RHYTHMS

24 h rhythms, regulated by biological clocks. For example, we go to sleep every 24 h, so sleep/wake cycles have a circadian rhythm.

SLEEP HOMEOSTASIS

Body mechanisms that control our need to sleep. It can be compared to a battery - when it is fully charged, we have more energy to carry out daily tasks; when it is empty, we have low energy and need to sleep to recharge the battery.

BIOLOGICAL CLOCKS

Internal clocks that regulate rhythmic cycles, like that of sleeping and waking.

HOW DO OUR BODIES KNOW WHEN TO SLEEP?

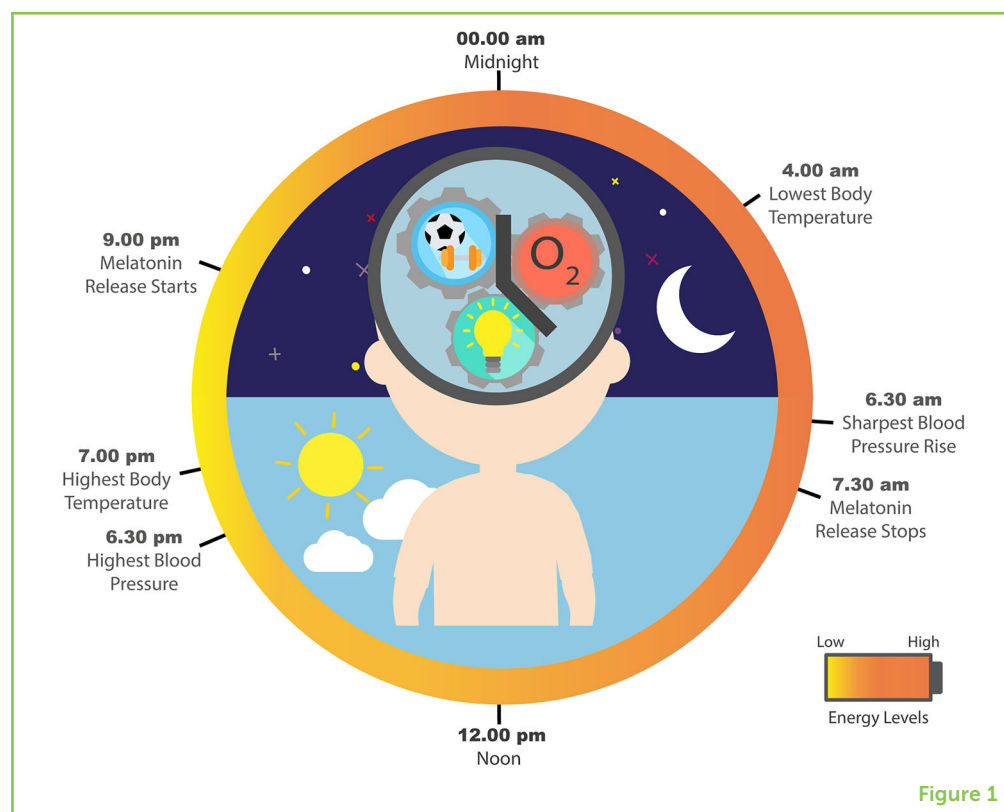
Sleep is a fundamental biological function, highly regulated by (1) **circadian rhythms**, which are 24 h cycles that regulate the internal processes of our bodies, and (2) **sleep homeostasis**, which is the “battery” that regulates our energy levels and tells us when to sleep and when to awaken.

Circadian rhythms are cycles of approximately 24 h (from the Latin *circa* — “about” — and *diem* — “a day”) that underlie all the biological and behavioral functions of our bodies. Each cell of the body acts as a **biological clock**, meaning that we all have multiple clocks inside our bodies, in all tissues and organs. These **biological clocks** organize the day into 24 h, assigning specific functions, such as sleeping, to specific times of the day [1]. The timing of these clocks is set by a master clock located in the brain. Biological clocks are also affected by the condition of the body, such as its energy level, and on factors in the external environment, such as the amount of light or oxygen that is present or the amount of physical activity that is being performed. One example of a function regulated by biological clocks is body temperature, which is highest between 4 and 6 p.m. and lowest around 4 a.m. Activity and sleep patterns are also regulated by biological clocks. During the day, we are usually more alert and active: eating, playing, working, moving, etc., while during the night, we are less active and more predisposed to sleep.

When the day starts, we are often full of energy, but this energy decreases as the day goes on and at night we feel more tired, because our bodies need to sleep. During sleep time, the body uses energy to perform maintenance and repair, recharging our batteries (Figure 1). Superman also needs to recharge his powers under the sun. So, we sleep when our biological clocks tell us to, and when our batteries are empty. We wake up when our batteries are fully charged. This cycle repeats every 24 h.

Figure 1

Day/night cycle of the body. During daytime, with sunlight, we are more likely to perform activities that require more energy from our batteries (orange represents high energy levels in the battery). Energy levels decrease throughout the day (yellow represents low energy in the battery), and at night, body temperature decreases and the brain produces a sleep signal called melatonin, telling us that we need to sleep to recharge our batteries.

**Figure 1**

SLEEP IS IMPORTANT!

Most people are not aware of the importance of having good sleep habits, and only a few sleep enough hours to recharge their batteries. Sleeping less than what your body needs, which is called sleep deprivation, has severe consequences. In the short term, sleep deprivation can cause irritability, poor memory, concentration problems, headaches, and decreased immune defenses. In the long term, sleep deprivation can lead to an increased likelihood of developing certain diseases, including heart disease, obesity, and brain disorders. This also happens to Superman—his powers diminish when he is not exposed to the sun for a long time. The necessary number of hours of sleep needed to fully recharge our batteries varies from person to person and from age group to age group. The National Sleep Foundation, an American organization created to improve health and well-being through sleep education, recommends a suitable number of hours for each age group (Figure 2) [2].

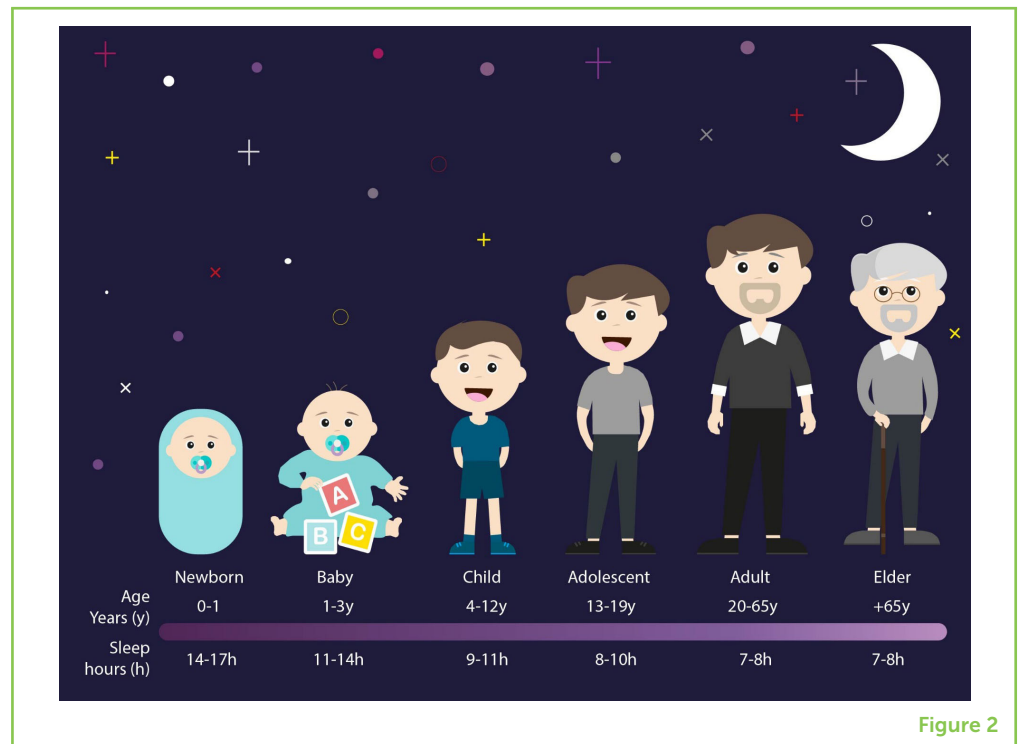
CHRONOTYPE

Inner time preferences, set by our internal clocks, that determine when we are alert and productive during the day, either in the early morning hours or later in the day.

Respecting the number of hours of sleep that our bodies need is very important. However, it is equally important to understand when we should sleep. Each of us has our own internal rhythm, called a **chronotype**, defined by our internal clocks. Our chronotype determines when we like to sleep [3]. Two main chronotypes, called morningness (being most active and alert in the mornings) and eveningness (being most active and alert in the evenings), are the two extremes. However, chronotype also changes as we

Figure 2

Recommended sleep hours by age group, according to the National Sleep Foundation. The age ranges and recommended hours of sleep are shown along the purple line at the bottom of the figure.



get older. Preteens and many elderly people usually experience morningness, while adolescents commonly experience eveningness. Indeed, many teenagers feel excessively sleepy during the day because they have difficulty falling asleep at night and waking up early in the morning.

WHAT IS SLEEP HYGIENE?

Taking too long to fall asleep, sleep disturbances, and daytime sleepiness are the most obvious signs of poor **sleep hygiene**. Good sleep hygiene includes habits and practices that help you to have a good night of sleep [4] (Figure 3). For example, going to bed and waking up at regular times. Even in exceptional cases, it is important to not go beyond 2 h from our regular routines, as it may deregulate our internal clocks and lead to difficulties falling asleep or waking up at specific hours. Physical exercise is also important to improve sleep quality. However, exercise acts as a stimulant and should be avoided close to bedtime. Similarly, other stimulants, such as chocolate and caffeinated drinks, keep our brains awake and should also be avoided close to bedtime.

Sleeping conditions should also be considered, such as the bedroom's temperature (16–18°C or 61–64°C), its comfort, and its lighting. Bright light from lamps, cell phones, and TV screens should be turned off and electronic devices should be left out of the bedroom. Even before going to bed, the excessive use of electronics and bright lights should be avoided. Why? At dusk, our brains start to prepare our bodies

SLEEP HYGIENE

Habits that lead to the right amount of sleep and good quality sleep.

Figure 3

Sleep hygiene. In order to have a good night's sleep, it is important to adopt sleep hygiene habits shown here.

**Figure 3**

MELATONIN

Called the sleep hormone; a chemical signal produced by the brain in response to the absence of light that makes us feel sleepy.

to sleep. The absence of intense light allows the production of a chemical signal that makes us feel sleepy. This chemical is called **melatonin**—the sleep hormone. Melatonin levels start to increase after sunset until the middle of the night (2–3 a.m.). Then, melatonin levels begin to decrease until dawn. When we use electronic devices, the screens' light tricks the brain into thinking it is daytime again—the blue light emitted by screens is perceived by the brain as sunlight. This phenomenon delays melatonin production and consequently delays the start of sleep, similar to the Metropolis city danger signals that make Clark Kent awaken as Superman. Preparing ourselves for sleep by avoiding stimulating light helps us to train our bodies to sleep better and healthier.

BE AWARE OF SLEEP DISORDERS

Sleep disorders can cause difficulties with falling asleep or staying asleep, affecting the quantity and quality of our sleep. There are over 80 diagnosed sleep disorders [5] (Table 1). These can be caused by irregular sleep schedules, caffeine or alcohol, drugs, aging, a genetic predisposition, or the presence of other medical conditions, such as anxiety or brain disorders. We can imagine these disorders as Kryptonite, which weakens Superman and puts Metropolis city into serious danger.

If good sleep hygiene does not improve ongoing sleep difficulties, consulting a medical doctor or a sleep specialist should be the next step. First, the medical doctor will talk with the patient and evaluate his/her sleep habits, sleepiness during the day, presence of diseases,

Table 1

Categories of sleep disorders and characteristics.

Sleep Disorder Categories	Characteristics
Insomnia	Most prevalent sleep disorder worldwide. It consists on the inability to fall or stay asleep and/or a poor-quality sleep.
Sleep-related breathing disorders	Involve difficulties in breathing during sleep, promoting frequent awakenings. It includes Obstructive Sleep Apnea.
Central disorders of hypersomnolence	Excessive sleepiness that is not caused by sleep problems or abnormal circadian rhythms.
Hypersomnia	Patients fall asleep at inconvenient or even dangerous places, such as at work or while driving.
Circadian Rhythm Sleep-Wake Disorders	The patient's sleep pattern (chronotype) is very early or very late, as Delayed Sleep Phase Syndrome.
Parasomnias	Unwanted movements, behaviours or dreams while falling asleep, sleeping or waking up. These include sleepwalking (somnambulism), a sleep disorder that is very common in kids. Sleepwalking means getting up and walking or carrying out activities while sleeping. Most kids have sleepwalking episodes occasionally and outgrow it by the teen years or when they reach adolescence.
Sleep Related Movement Disorders	Conditions that cause simple involuntary movements, as leg movements, that disturb sleep or its onset.
Other sleep disorders	Other disturbances that do not fit into any of the classification sections above but that impact on sleep, such as sleep disturbances associated with other medical conditions.

Table 1

and current medication. If bad sleeping habits are detected, the doctor will advise the patient to change those habits to promote better sleep hygiene. If bad sleeping habits are not the problem, the patient must be further evaluated. Sleep might be monitored at home or at a Sleep Unit, using electronic devices. If a sleep disorder is diagnosed, there are several treatments that might be followed depending on the diagnosis. For example, a medical doctor might prescribe medication containing melatonin, if indicated. The status of the patient will be monitored by the Sleep Unit throughout the treatment and, depending on how the patient does, medication can be adjusted or removed. Other treatments might involve wearing devices during sleep, such as masks that help breathing while sleeping, or a psychologist to help people to sleep better.

To finalize, we recommend you to see this video where you can review all about sleep!

Video—Animation on the importance of sleep, developed together with the Portuguese Sleep Association.

SLEEP WELL, SLEEP TIGHT

Now that you know how, when and why our bodies need to sleep, habits and practices that help to sleep better or that, on the contrary, disturb a good sleep night, existent sleep disorders and what to do in those contexts, there are no excuses to not have a good night of sleep! Do not let a bad sleep night be your kryptonite, superhero!

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SUBMITTED: 03 March 2020; **ACCEPTED:** 03 November 2020;

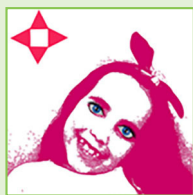
PUBLISHED ONLINE: 01 December 2020.

EDITED BY: Laura Ferraro, University of Palermo, Italy

CITATION: Gaspar LS, Santos B, Barros-Viegas AT, Cardoso J, Varela Amaral S, Carvalhas-Almeida C, Santos-Carvalho A, Cavadas C and Álvaro AR (2020) The Superpowers of Our Sleep. *Front. Young Minds* 8:540052. doi: 10.3389/frym.2020.540052

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YOUNG REVIEWERS

ALBA, AGE: 8

My name is Alba. I am 8 years old and I am from Córdoba, Spain. My hobbies are dancing, singing, cooking, and playing with my brother. When I am older, I want to be either a teacher or a singer, a dancer, or an actress.

MARTINA, AGE: 8

My name is Martina. I am 8 years old and I am from Spain. My hobbies are drawing, listening to pop music, and skating. When I am older, I want to be a teacher or a famous painter.

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Laetitia Gaspar received a Bachelor's degree in Genetics and Biotechnology from the University of Trás-os-Montes e Alto Douro (2014) and a Master's in Cellular and Molecular Biology from the University of Coimbra (2016), Portugal. Laetitia has since been working in the sleep field, on Obstructive Sleep Apnea (OSA), one of the most common but highly undiagnosed sleep disorders. For her Ph.D., Laetitia is exploring OSA's impact on cells, while searching for new strategies to improve OSA diagnosis. She has also been actively involved in several initiatives to improve awareness of the importance of sleep.

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Catarina Almeida has a Master's in Cellular and Molecular Biology from the University of Coimbra. She has worked on several neuroscience related projects at the Champalimaud Foundation Center for the Unknown and Institute of Molecular Medicine, both based in Lisbon, Portugal. Now she is devoted to studying sleep disorders, and in particular, the search for biomarkers to help diagnose sleep apnea obstructive syndrome, at the Center for Neurosciences and Cell Biology of Coimbra, Portugal. She is also committed to communicating science to society and helping to raise awareness of the importance of sleep.



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Ana Santos-Carvalho is a Ph.D. researcher and science communicator in Health Sciences. Ana studied the protective role of a brain signal in the retina (the back of our eye that senses light and sends information about it to the brain). After her Ph.D., she developed an interface between schools and research centers in Portugal's Institute for Education and Citizenship. Later, she began working with a research team studying sleep disorders. Currently, Ana is coordinating science communication at Institute for Interdisciplinary Research at the University of Coimbra.



CLÁUDIA CAVADAS

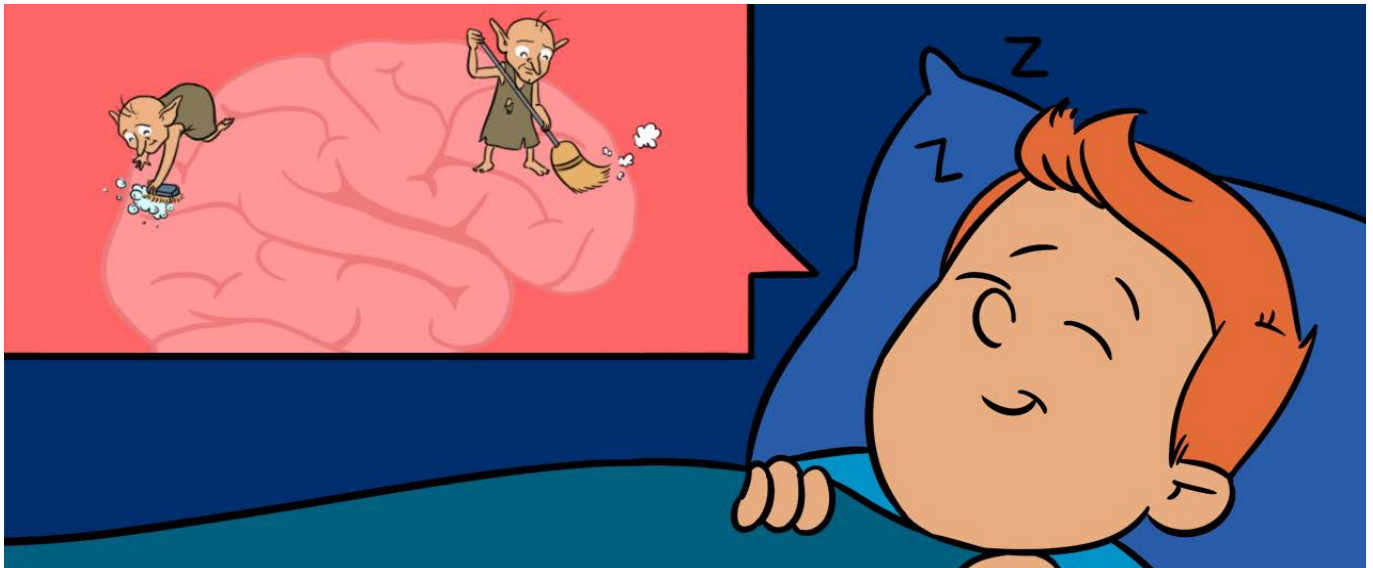
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DO HOUSE-ELVES CLEAN YOUR BRAIN WHILE YOU SLEEP?

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REVIEWED BY:



**EXPLORA
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MUSEUM**
AGE: 7–15

NEUROSCIENTISTS

Scientists who study brains and nervous systems.

Sleep will consume one-third of your life. You can't avoid it, nor should you. Sound slumber can make you feel wonderful. But there's more to it. Sleep is also essential for learning. Much of who you are—your memories and your habits—may depend on what your brain does while you sleep. This article covers some new experiments on this topic, and some unexpected findings. Each day, you acquire all sorts of new knowledge. That includes things you read, things you learn in school, news about friends, and your own creative thoughts or pictures. And maybe where you put down that book you were reading. Later, many of these memories can be difficult to remember. Recent scientific findings are helping us understand how brain activity during sleep aids remembering.

The brain is far from idle when we sleep. No one knows exactly why. Put a computer to sleep, and it simply stops and does nothing. Not our brains. Yet, we wake up knowing very little about what our brains have been doing.

Neuroscientists have many ways to observe brain activity. And they have conjured up many explanations for these mysterious goings-on inside the sleeping brain.

Here's one idea. Picture a house-elf, busy the whole night, just like in Harry Potter's world. The author J. K. Rowling portrayed the house-elf as a creature who worked like a slave in the house of a wizard, each night invisibly cleaning up the mess the wizard made during the day. But this "house-elf-of-the-brain" would instead work to strengthen valuable memories and squash unimportant ones. Can you imagine a group of miniature house-elves organizing memories in your brain in this way? Perhaps that's how memories end up in good working order the next morning.

Yes, that's a fantasy, not neuroscience. But our brains face a big challenge. We need to hold on to important memories, and for that to happen, it helps to forget the unimportant ones. So, something like magic is needed to make learning succeed.

Each day, countless memories are stored in your brain. Before long, they may all be forgotten. Pick a day from the middle of last week. How much can you remember about that day right now? Chances are, most of the memories you created that day have already disappeared (or as Harry Potter might say, "disapparated").

What if you want to counteract this memory loss? You already know what to do! You practice what you've learned. It's the same thing actors do when they rehearse their lines in a play.

When you want to memorize something, bring it to mind and rehearse it, repeatedly.

One of the big challenges in **Cognitive Neuroscience** is to explain how new information gets into your brain. We are also investigating how rehearsal helps. The effort you spend working to remember pays off. The reason is that **brain networks** change when you use them. So, when you remember something, that memory gets stronger.

But that's not the only way to select memories to strengthen. It also happens while we sleep. We don't need to plan to rehearse memories during sleep. We do so naturally, and we wake up with no awareness of doing so.

LISTEN FOR THE TONE

A recent scientific breakthrough helped connect memory and sleep. It involved a series of experiments with sounds. If a flute plays a soft tone while a person is learning a fact, the sound and the fact can be linked. Later, during sleep, that flute sound can be soft enough to not awaken the person but still remind them of the fact. When this happens, the brain networks involved in remembering the fact change.

COGNITIVE NEUROSCIENCE

That part of neuroscience engaged with investigating mental functions.

BRAIN NETWORKS

A set of brain cells (neurons) that can be active together. Learning involves changes in such brain networks. Neuroscientists use the term "neural plasticity" to refer to these changes in how neurons in a network are connected with each other.

Most scientists studying sleep used to think that hearing didn't work very well during sleep. That view wasn't quite right. In 2009, my students and I discovered that soft sounds could be used to investigate memory rehearsal during sleep [1]. We concluded that the sounds worked as "memory reminders," because they changed the storage of recent memories.

Scientists working in several different countries have now repeated this type of experiment many times [2]. Usually, students play a key role. In our experiment, students first learned where 50 pictures appeared on a computer screen. For example, they might see a flute in the upper left corner and a stapler in the lower right. Each picture appeared together with a specific sound. This learning was not much fun compared to playing a video game, but the students cooperated anyway and learned all the locations. Next, each student took a nap. After they woke up, we tested them to see what they remembered. They had to recall exactly where they had seen each picture. We measured where they placed it on the screen. The closer they placed each picture to the spot where it belonged, the better they scored on this memory test.

For some of the pictures, the specific sounds that came with them were played during the nap. The students slept right through this. They didn't know that any sounds were played.

We compared recall for those pictures and the remaining pictures (for which the sound was not played during sleep). Recall was better for pictures when their sounds were played during sleep. When the sounds played, memory storage in the brain must have changed (see Video 1). This general experimental procedure (see Figure 1) thus allows neuroscientists to hack into memories.

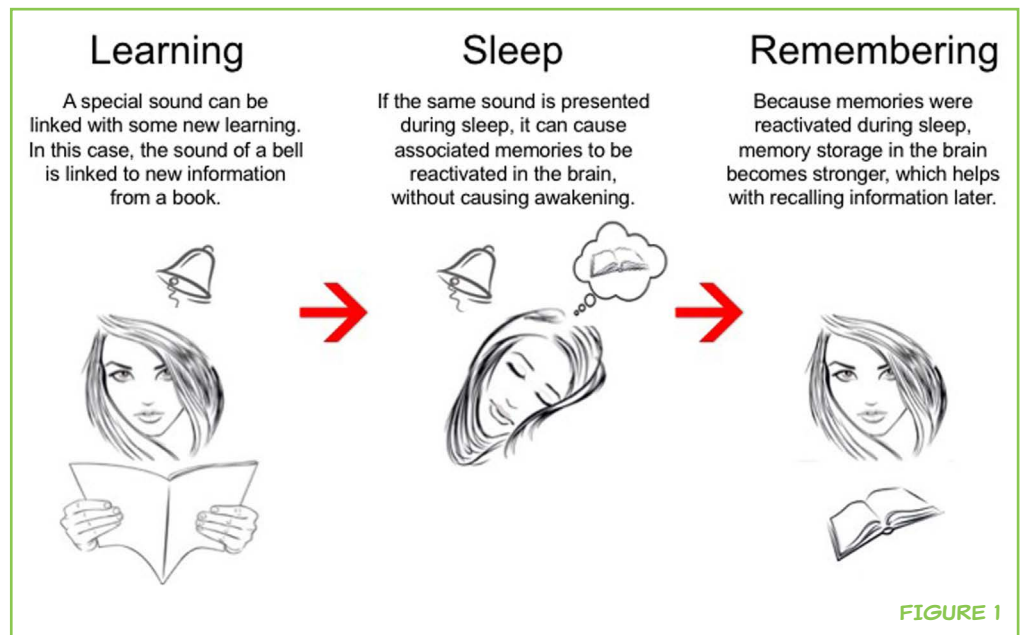
VIDEO 1

Targeted Memory Reactivation. This video segment was produced through the National Science Foundation and their Science Nation team. http://www.nsf.gov/news/special_reports/science_nation/sleepmemory.jsp



FIGURE 1

The experiments described here typically have three parts. First, people learn some new information. The new information can be from a book, or it could be about where objects are located, what foreign words mean, or how to perform a piece of music. Second, during sleep, that information may be reactivated so that it is stored in the brain more effectively. A sound of a bell, for example, can remind the sleeping brain of information from a book, if the bell was also ringing during learning. Similarly, a smell can be present when learning is accomplished, and then presented again during sleep. Memory reminders during sleep increase the likelihood that the information is firmly memorized. In the third part of the experiment, there is a memory test. Remembering is improved for information that was reactivated. These experiments help us to understand the normal process of learning. It seems that when we sleep every night, our brains are busy practicing and recalling the new things we've learned. Of course, it is also helpful to rehearse memories when we are awake. Why memory rehearsal might be particularly helpful during sleep is presently unclear, although the brain produces intriguing electrical signals that seem to hint at what's going on inside. These and other mysteries are waiting to be solved by the neuroscientists of the future.

**FIGURE 1****MEMORY HACKING**

This research moves us forward in understanding how memories are stored in the brain. The findings also raise a wild possibility. Maybe people could select memories to reactivate while sleeping at home. Why do this? One reason is that we may not get enough sleep. And even when we do, sleep may not work perfectly. We may unknowingly rehearse things we'd prefer to forget. Is your sleep filled with any annoying memories? Perhaps you could rehearse what you really want to remember instead.

There are many possibilities for using sleep to improve learning. In 2015, researchers helped students to learn a foreign language using the same basic method [3]. Students first spent some time learning Dutch words. Some of those words were presented again later, when the students were asleep. When they woke, they knew the meanings of the words presented while they were asleep better than for those not presented while they were asleep. In a similar study, we improved the learning of rules of grammar important for learning a new language [4]. We also strengthened musical skills during sleep [5]. In that study, students first learned to perform two songs on a keyboard. It was like the Guitar Hero videogame: moving circles guided the students to press keys in the proper way to produce each song. Then came a nap. Afterward, the students were better at playing the song that had been quietly presented to them while they slept.

We learn some skills and habits without knowing that we are learning them. The technical term for this type of learning is **implicit learning**. One example is the bad habit of teeth grinding during sleep. If you do that, how can you learn to stop? It can be difficult to control what you only do while you are sleeping.

IMPLICIT LEARNING

A type of learning that happens without people realizing what they have learned. After this learning, as in gaining a skill, habit, or procedure, people may think and behave differently without realizing that their thoughts and behaviors have been changed by implicit learning.

UNCONSCIOUS SOCIAL BIAS

A kind of habit learning in which we acquire general ideas about groups of people. These biases then influence how we treat others, sometimes unfairly, and even when we don't realize that our behaviors are governed by this learning.

Our idea is that special sounds played during sleep might help. First, people would learn to release their jaws when hearing the “relax sound” during the day. That same sound could then cue them to relax the jaw during sleep.

New ideas like this need to be tested. We don't know yet whether they will work. But we are hopeful because of various other experimental results. For example, our sleep method helped with another habit when we used it to reinforce training to reduce prejudice [6].

To understand our experiment, consider the following. We all gradually pick up general beliefs about groups of people from exposure to movies, TV, and the like. This is a natural part of learning. We can pick up such ideas (generalizations) without knowing it, and even without agreeing with the ideas. The ideas can then influence our thoughts and behaviors toward people in those groups. Here's one specific example. Long ago, a common stereotype was that women were not smart enough to be scientists. Scientists in movies and on TV were often played by actors who were old, bald, white men. Exposure to that stereotype can produce an **unconscious social bias**. This type of bias about a group of people regularly influences how we treat other people, and we needn't be aware of this influence. But like other types of learning, these habits of bias can be changed by training. For example, the repeated experience of meeting women who are amazing scientists can reduce the bias you might get from the media. Our experiment showed that memory reminders during sleep can reinforce training to reduce common biases about people.

Research might also produce ways to achieve other valuable benefits using memory reminders during sleep. For example, learning can be really important after someone suffers brain damage. The patient may need to recover the ability to speak or to move normally. Rehabilitation sessions aim to speed learning in certain brain networks. Recovery depends on how well this learning progresses. With only a few hours of therapy a week, it can take a while for this rehabilitation to work. Sleep-assisted therapy could use sounds associated with the actions the patient is trying to learn. Playing those sounds nightly might speed the person's recovery. Future experiments will hopefully show how to make this work.

CAN MEMORY HACKING BE HARMFUL?

New ways to modify memories could have a cost. So far, I've emphasized ways to help people. But could these methods also harm people?

The author Aldous Huxley imagined how bad things could go in his novel, *Brave New World* [7]. In this story, the state controlled its citizens through what Huxley called “hypnopedia.” That is, when infants and children slept, they were taught certain ways to think. Everyone was assigned a specific role in society, some high and some low. And they were all persuaded to

buy things and be eager consumers. Because of their training, people in this world seemed to have no choice but to take on their duties and to accept their assigned status.

We should proceed carefully with new technology. People do not want their memories to be altered during sleep without their permission. Abuse of this method might be possible. For example, an unethical hotel owner could play messages to hotel guests while they sleep. The guests might receive unwanted advertising without even knowing it. We need to be watchful so methods for changing memories during sleep are not abused.

In the experiments I've described, the procedure required some training. People were always awake during this training and what they learned wasn't hidden from them. One way for a person to avoid unwanted memory changes during sleep is to exercise the option to reject what is being taught in the first place.

Neuroscience has opened the door to new possibilities for guiding the sleeping brain to work better. In a sense, it's as if house-elves really do clean your brain while you sleep. With further scientific efforts in these new directions, a better understanding of the sleeping brain could bring many different benefits. Ideally, this research will give us more reasons to treasure—rather than resent—our need for sleep.

ACKNOWLEDGMENTS

Some of the research leading to these results received funding from the National Science Foundation. I am grateful to my many collaborators in this research, and to my friends Marcia Grabowecky, John Kounios, and Lisa Munoz for their help with the writing. This article is based on an article that originally appeared on LiveScience.com.

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SUBMITTED: 12 December 2017; **ACCEPTED:** 11 May 2018;

PUBLISHED ONLINE: 22 June 2018.

EDITED BY: Kathleen Haaland, University of New Mexico, United States

CITATION: Paller KA (2018) Do House-Elves Clean Your Brain While You Sleep? *Front. Young Minds* 6:23. doi:10.3389/frym.2018.00023

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REVIEWED BY

EXPLORA SCIENCE CENTER AND CHILDREN'S MUSEUM, AGE: 7–15

The Explora Young Minds reviewers are a group of science enthusiasts working with museum educators and mentors from the University of New Mexico. We enjoy learning about the brain through the articles and hands-on activities and demonstrations. We also enjoy reading about new research, asking questions, and making suggestions to help the scientists make their work more understandable for everyone!

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I am a professor at Northwestern University, which is next to Lake Michigan in Evanston, IL, USA. I enjoy the challenge of designing experiments that can provide insights into memory and our conscious experiences. I also enjoy my hobby of playing in a rock-and-roll band. I feel very fortunate that my day job involves wondering about how human minds work. I'm hopeful that our collective efforts to gain neuroscientific knowledge will contribute to improving people's lives. *kap@northwestern.edu.





WHAT CAN A BLIND FISH TEACH US ABOUT SLEEP?

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YOUNG REVIEWERS:



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AGES: 8–14

Nearly all animals studied to date sleep. It is widely accepted that sleep is critical for survival, yet the function of sleep remains unclear. Mexican cavefish have adapted in several ways for life in caves, but they have also evolved to sleep less than surface-dwelling fish. These fish are being used by scientists to investigate how sleep is regulated in response to an animal's environment. This article describes various experiments that can be conducted using cavefish to study sleep, and why these experiments might be useful to humans. The results of these experiments suggest that differences in sleep are influenced by a substance called hypocretin. Experiments, such as these help researchers to better understand how sleep has evolved over time and how to develop treatments for people suffering from sleep disorders.

INTRODUCTION

Sleep is a nearly universal behavior that has been defined in animals ranging from jellyfish to humans. Scientists regularly use animal

Figure 1

An introduction to the Mexican cavefish. (A) Surface- and cave-dwelling fish are found in the Sierra de el Abra region of northeast Mexico. (B) A diagram of a typical cavefish. Both surface- and cave-dwelling fish use their mouth, nose, and lateral line to sense their environment. However, because the cave-dwelling fish have no eyes, they must rely more heavily on these senses. (C) Surface fish live in the rivers of Mexico and southern Texas. These fish have normal eyes and pigmentation. (D) Pachón, (E) Molino, (F) Los Sabinos, and (G) Tinaja cave populations all have smaller eyes and reduced pigmentation, despite having evolved separately. Colored dots correspond to the locations of the caves shown in (A).

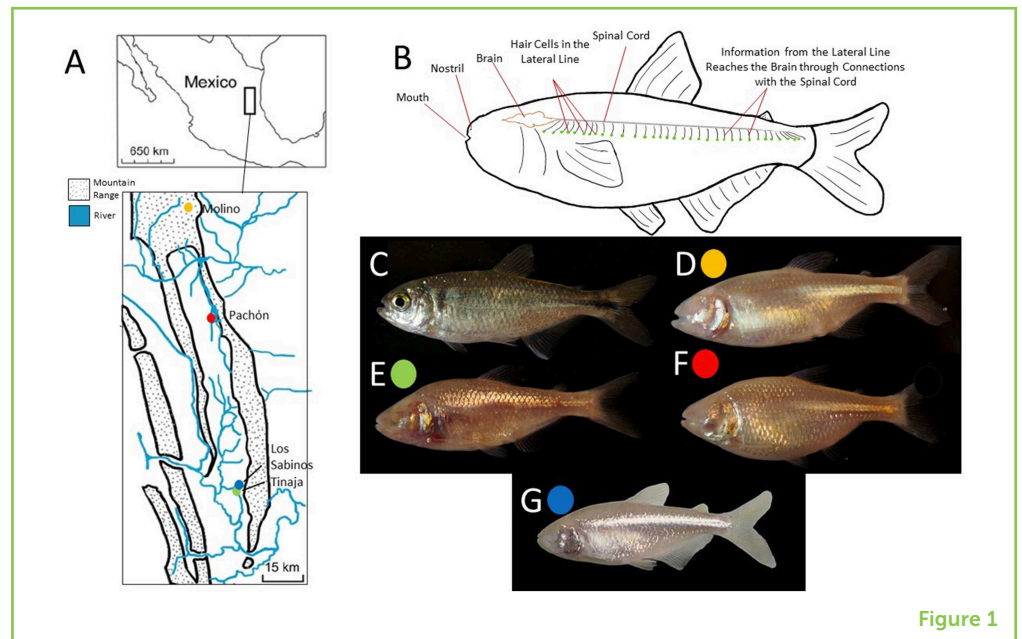


Figure 1

models, like fruit flies, zebrafish, and mice, along with sophisticated tools to alter genes, to study how the brain regulates sleep. These studies have found the genes and neurons (nerve cells) that control sleep are similar in all types of animals, suggesting that sleep has an ancient function that is critical for survival. Despite these findings, the function of sleep remains poorly understood. A central question for scientists is understanding how sleep evolves in different environments, and why some species, like elephants, only need a few hours of sleep each day while others, like armadillos, sleep most of the day [1].

Questions of evolution can often be addressed by identifying animals that have big differences from other animals, like those that need excessive or reduced amounts of sleep, and investigating the genes that play a role in these differences. Simple animals, like small fish, are often used in research on behavior, because their small size makes these experiments easier. The Mexican cavefish (scientific name **Astyanax mexicanus**) is especially useful for studying the evolution of behavior, because different populations of these fish have dramatic behavioral differences, from river-dwelling surface fish of the same species. These fish exist as at least 29 eyeless populations that live in caves and as eyed surface fish that live in the rivers of Mexico and Southern Texas (Figure 1) [2]. The cave-dwelling populations are probably surface fish that became trapped in the caves, resulting in eventual changes to their appearance and behavior. Despite being from completely different caves, the cave-dwelling populations evolved many of the same characteristics. Some of these characteristics are due to differences in brain structure and activity that have evolved to help the cavefish better cope with the cave environment. One interesting difference between the cave- and

ASTYANAX MEXICANUS

A fresh-water fish found in the rivers of Mexico and southern Texas. Blind populations of these fish are found in limestone caves in northeast Mexico.

surface-dwelling populations of Mexican cavefish is in the amount of sleep each population gets. Cave-dwelling fish sleep significantly less than surface fish [2]. Because the populations are all the same species, they share many of the same genes, which makes it easier for scientists to identify the specific genes that cause the differences between the two populations. In this article, we will discuss how cave- and surface-dwelling populations are used to study the evolution of sleep and why this research may shed light on the genes that control our own sleep habits.

LIFE IN A CAVE

There are some obvious differences between the rivers and caves inhabited by the different populations of *A. mexicanus*. Perhaps the most obvious is the lack of light in the caves, which are hidden from sunlight. The constant temperature in caves and the lack of sunlight prevents plant growth, which would normally form the bottom of the food chain. The two major sources of nutrition within the caves are probably bat droppings and nutrients that are swept into the caves during seasonal flooding [3].

The lack of light has another significant effect on cave inhabitants: eyes are not particularly useful. We believe that, when fish were first trapped in caves, those with smaller eyes were more likely to survive and produce offspring because smaller eyes helped them to save energy. After many generations, survival of fish with smaller eyes eventually resulted in fish that completely lack functional eyes [2]. Mexican cavefish and other organisms that lost their eyes this way rely on their other senses instead, like smell, taste, or sensing waterflow. Scientists wonder whether eye loss, and the changes in other senses that accompany eye loss, influence the amount of sleep cave-dwelling fish need.

WHY DO CAVE-DWELLING FISH SLEEP LESS?

Lab experiments have shown that surface fish sleep about 6 h per day, while cave-dwelling fish sleep <2 h per day (Figure 2) [4]. Why did cave-dwelling fish evolve to spend less time sleeping? One possibility is that cave-dwelling fish have evolved to sleep less as a way of dealing with nutrient limitation. As we discussed above, in caves, there are no plants for the fish to eat and nutrients may not always be readily available. Sleeping less allows the fish more time to search for food. Cave-dwelling fish will also sleep more when their **lateral line**, a major sensory organ that detects prey, is made non-functional [5]. The lateral line consists of hair-like structures connected to neurons that detect vibrations or flow in water (similar to pressure receptors in human skin) and transmit this information to the brain. Because the lateral line is believed to be the major sense used by cave-dwelling fish to find food,

LATERAL LINE

An organ used by fish to sense their environment. The lateral line is made up of collections of hair cells. When water pressure around the fish changes, the moving water causes these hair cells to move and send a signal to the fish's brain. The fish can use this information to get a sense of its surroundings.

Figure 2

Measuring sleep in cavefish. **(A)** Either a cave- or surface-dwelling fish is placed in a tank and their behavior is recorded. These recordings are analyzed using computer software that tracks the activity of the fish. When the fish go at least a minute without moving we can assume they are sleeping. **(B)** Measuring the sleep duration over 24 h reveals sleep in surface-dwelling fish (black) is reduced compared with Pachón cavefish (blue) during the day and night. The shaded portion of the graph shows when the fish are in the dark (to simulate the natural day-night cycle).

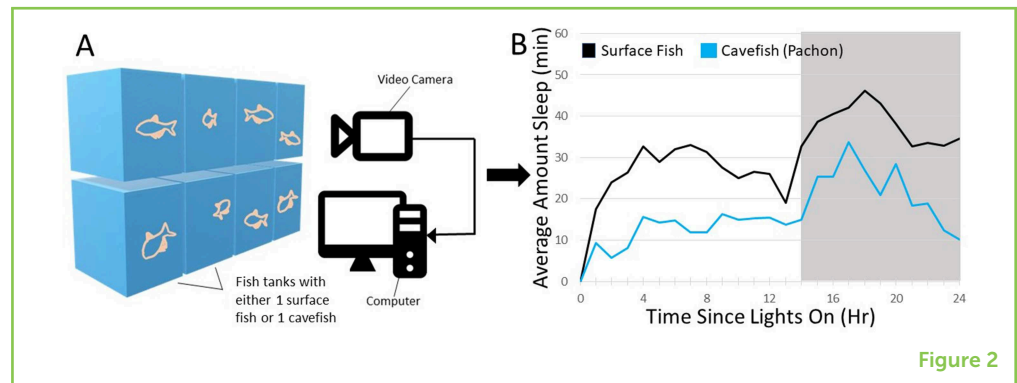


Figure 2

this supports the idea that nutrient availability has played a part in the evolution of this difference in sleep.

Our ability to prove or disprove this hypothesis is limited by our lack of complete understanding of the fish's natural environment. In the lab, fish are raised under constant, controlled conditions that are very different from the conditions of a river or cave. In the lab, fish are kept in standard fish tanks with light provided for 10 h each day. While keeping both types of fish in the same conditions is essential for experiments comparing surface- and cave-dwelling fish, this procedure may not reflect the animal's natural environment. For this reason, scientists are organizing expeditions into the caves to gather data on how things like temperature and nutrient levels vary over time. These experiments are difficult, because the caves are isolated and often difficult to access. Further, measuring sleep behavior in the wild is especially challenging. In a recent expedition, we collected water samples from several caves and will compare the DNA in the water, which will tell us about the animals and plants that live in each cave. Using information taken from cave expeditions, scientists will be able to better understand the significance of lab findings and design new experiments to test the effects of specific environmental factors, like food availability or temperature, on the evolution of different sleep patterns in surface- vs. cave-dwelling fish.

FLUORESCENCE

The emission of light. Some proteins, like those found in jellyfish, will emit light when they are exposed to light of certain colors. Scientists use fluorescent proteins to mark specific cells or brain regions, and then observe those cells or regions under a microscope.

WHAT KIND OF TECHNIQUES CAN WE USE TO STUDY SLEEP IN CAVEFISH?

Scientists often identify differences in brain function using sophisticated ways of looking at the brain. One way is by using **fluorescence**, meaning chemicals that emit light, to label parts of the brain that have specific types of neurons. Essentially, scientists take a fluorescent gene (usually from jellyfish) and use special techniques to have it produced in specific types of neurons in the fish. This technique causes the target neurons to glow under a special type of microscope. Scientists can then look for differences in the size, shape, or number of neurons in the cave-dwelling vs. surface-dwelling fish. These types of differences in

Figure 3

Levels of the small protein hypocretin (hcr), which prevents sleep, are increased in cavefish. **(A)** To measure hypocretin levels within the brain, the brain is dissected out of the fish and then sliced. The brain slices are then labeled with a fluorescent chemical so the cells can be seen using a special microscope. **(B,C)** Comparing brain slices from surface-dwelling fish **(B)** and cave-dwelling fish **(C)** show that levels of hypocretin protein (HCRT, green) are higher in cave-dwelling than in surface-dwelling fish. **(D)** The number of HCRT neurons is greater in cave-dwelling fish and blocking hcr activity in cave-dwelling fish caused them to sleep more. Blocking hcr activity in surface fish did not influence their sleep. Adapted from Jaggar et al. [6].

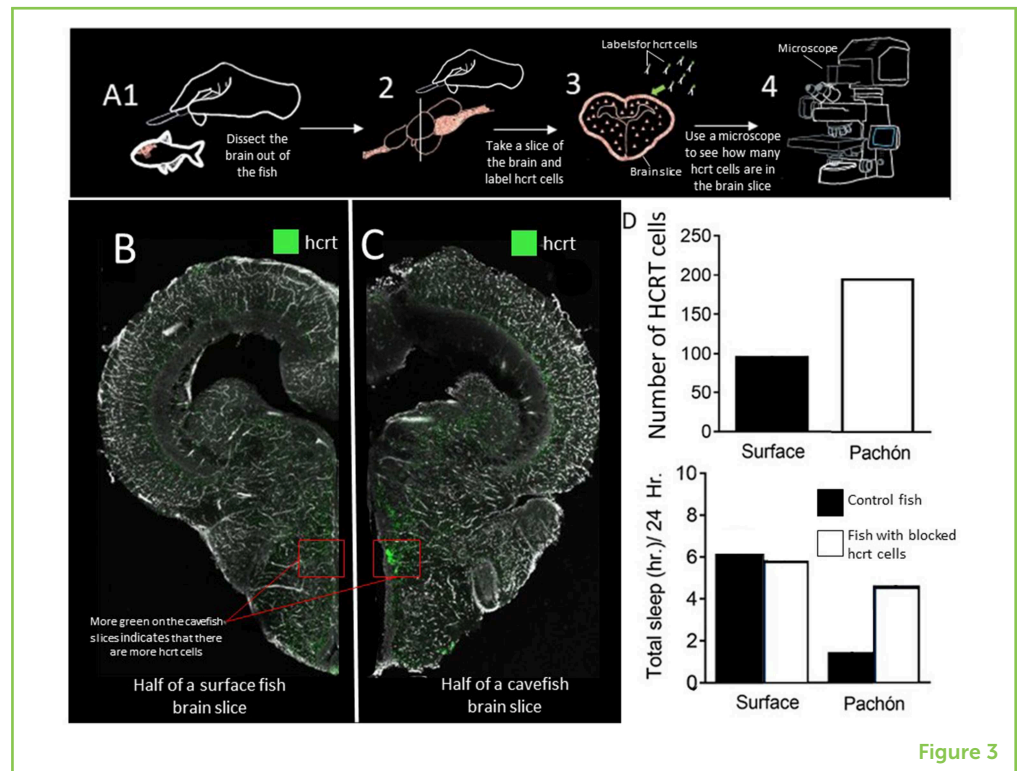


Figure 3

neurons between the populations can provide clues to how the brain is regulating the behavior of the fish. For example, we used fluorescence to label the neurons that produce **hypocretin**, a small protein that prevents sleep. We found that cave-dwelling fish brains have more neurons that produce this peptide than surface-dwelling fish brains (Figure 3) [6]. These findings suggest that hypocretin may have evolved to reduce sleep in cave-dwelling fish.

Because cave-dwelling and surface-dwelling fish are so similar, comparing their **genomes** (all of their genes) is a powerful way to identify genes that might be controlling different behaviors, like sleep. Once a gene of interest has been identified, scientists can use special techniques to delete, modify, or insert genes into fish embryos, to create genetically modified animals [7]! For example, these techniques have been used to reduce hypocretin in the brains of cave-dwelling fish, which resulted in increased sleep [6]. Doing the same experiment in surface-dwelling fish, however, had no effect. These data strengthen the possibility that hypocretin is involved in the difference in sleep between cave- and surface-dwelling fish.

Scientists can also breed cave-dwelling fish with surface-dwelling fish, to create hybrid fish that are interesting to study. These fish have variable appearance and sleep duration. By testing each fish for sleep and then sequencing its genome, a process called **quantitative trait loci** mapping, scientists can identify regions of the genome (and sometimes individual genes) that regulate sleep [8]. For example, if a scientist tests 2,000 fish and most of the fish that do not sleep share a

HYPOCRETIN

A small protein secreted by neurons to communicate with other neurons. Hypocretin promotes wakefulness. Humans and dogs that lose hypocretin function develop a sleep disorder called narcolepsy.

GENOME

All of the genes and genetic material within an organism.

QUANTITATIVE TRAIT LOCI

A statistical analysis that associates a specific genetic change with a trait, like sleep or eye size.

certain gene, this gene would be identified as potentially contributing to sleep. That gene could then be studied in more detail to investigate how it influences sleep.

Another powerful technique to study sleep in cavefish is drug screening. Fish are bathed in different drugs, to try to find drugs that can make cave-dwelling fish sleep more.

Together, these techniques for studying sleep in cavefish can help us to understand why cave-dwelling fish sleep less than surface-dwelling fish. While we have learned a lot about the sleep differences between these two types of fish, there is still a lot of work to be done!

WHAT CAN CAVEFISH DO FOR US?

There is significant variation in sleep across the animal kingdom. For example, elephants only sleep 3–4 h per day, while brown bats sleep about 20 h per day. Even among humans there is variation in sleep, with some people getting <5 h and others getting more than 10 h. Despite this variation, regulators of sleep are the same in different kinds of organisms, including people and cavefish. Hypocretin, for example, has been associated with human sleeping disorders. For this reason, understanding how sleep is regulated in cavefish can help scientists understand how sleep is regulated in humans. Animals like cavefish can help us understand not only why there is so much variation in sleep among people, but also the mechanisms behind various sleep disorders. Further, cavefish could be used to screen for drugs to test whether those drugs might work for sleep disorders in people.

ORIGINAL SOURCE ARTICLE

Jaggard, J. B., Stahl, B. A., Lloyd, E., Prober, D. A., Duboue, E. R., and Keene, A. C. 2018. Hypocretin underlies the evolution of sleep loss in the Mexican cavefish. *eLife* 7:e32637. doi: 10.7554/eLife.32637

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SUBMITTED: 01 February 2019; **ACCEPTED:** 16 July 2019;

PUBLISHED ONLINE: 02 August 2019.

EDITED BY: Kathleen Y. Haaland, University of New Mexico, United States

CITATION: Paz A and Keene AC (2019) What Can a Blind Fish Teach Us About Sleep? *Front. Young Minds* 7:103. doi: 10.3389/frym.2019.00103

CONFLICT OF INTEREST STATEMENT: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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YOUNG REVIEWERS

EXPLORA SCIENCE CENTER AND CHILDREN'S MUSEUM, AGES: 8–14

The Explora Young Minds reviewers are a group of science enthusiasts working with museum educators and mentors from the University of New Mexico. We enjoy learning about the brain through the articles. We also enjoy asking questions and making suggestions to help the scientists make their work more understandable for everyone! We were helped by our Science Mentor Jennifer Walter. She just received her Ph.D. in pediatric neuropsychology. She enjoys working with kids, playing with her dog, and trying to cook new recipes.



AUTHORS



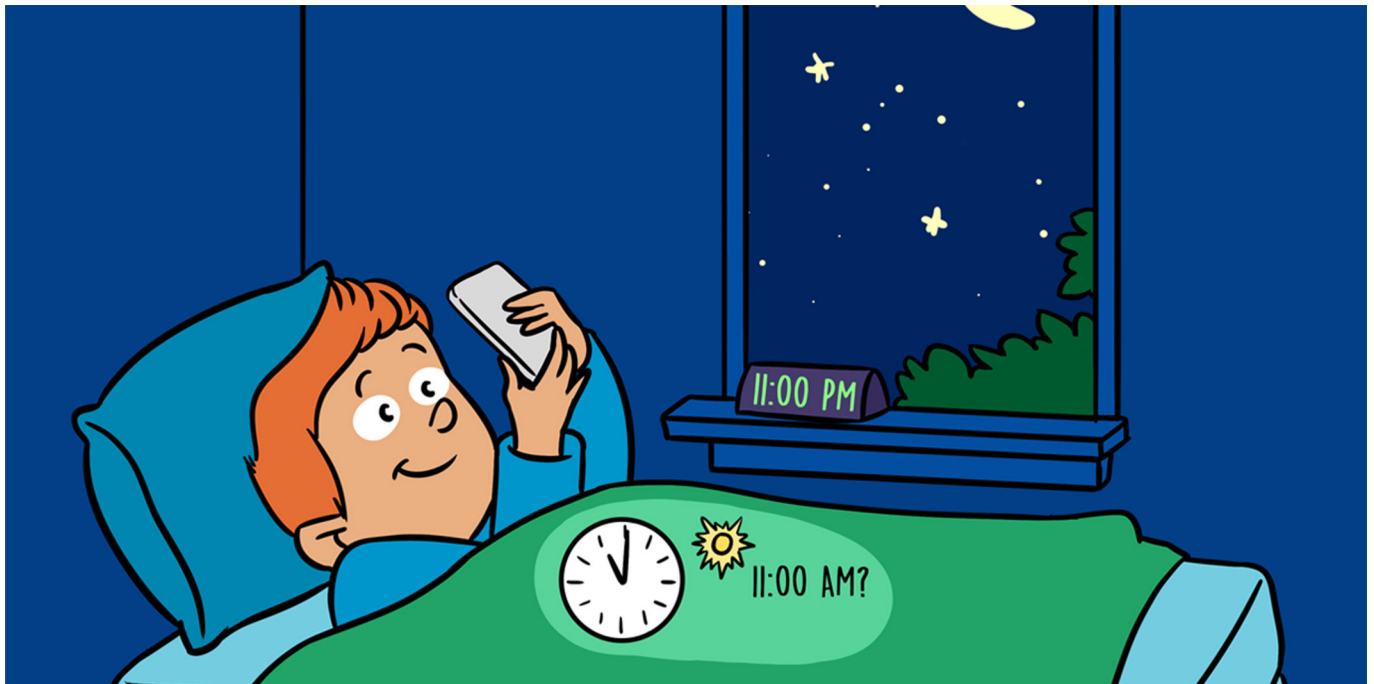
ALEXANDRA PAZ

I am a Ph.D. student studying neuroscience at Florida Atlantic University. After graduating from St. Bonaventure University with my Bachelors in Biology, I worked as a hydrologic technician in Everglades National Park. Right now, I am working toward getting my Ph.D. so that one day I can have my own lab to conduct research and give students of all ages the opportunity to experience how exciting science can be. When I am not in the lab I like to swim, boat, and play video games.



ALEX C. KEENE

I am an Associate Professor of Biological Science at Florida Atlantic University where I direct the summer Research Experience for Undergraduates (REU) and Neuroscience B.S. programs. I received my Ph.D. from UMass Medical School in 2006 where I studied how memories are formed in fruit flies. My lab studies many different aspects of neuroscience including memory, sleep, taste, and aging. I find that the best part of science is the collaboration and teamwork that takes me all over the world. *alexckeene@gmail.com



HOW DO OUR CELLS TELL TIME?

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YOUNG REVIEWERS:



LAURI

AGE: 16



TUOMAS

AGE: 15

BIOLOGICAL CLOCK

A molecular mechanism that keeps track of time within the cells of an organism, and gives rise to circadian rhythms.

Did you know that your cells can tell the time? Every cell in your body has its very own clock. These clocks are unlike any other. There are no cogs or gears. The time is set by the rotation of the Earth, so that our bodies are perfectly aligned with night and day. While you may not even be aware of their existence, these clocks control many aspects your life. From when you eat and sleep to your ability to concentrate or run fast, the clocks command all. How do these clocks work and how do they tell the time? What happens to our clocks if we watch TV late at night or fly to the other side of the world? This article examines these questions and explains the scientific discoveries that have helped us to understand the answers.

THE BIOLOGICAL CLOCK

Our cells learned to tell the time before we did. Every cell in our bodies has its very own clock. Unlike the clocks we are used to, the clocks in our cells have no cogs or gears: they are biological. Our **biological clocks**

CIRCADIAN RHYTHM

Any process in an organism that falls into a 24-h rhythm or cycle.

keep near perfect time with the 24-h cycle of light and dark on Earth. We call this regular daily cycle the **circadian rhythm**. The word circadian comes from the Latin *circa* and *dies*, meaning “around the day.” The circadian rhythm aligns our sleep-wake cycle with the light-dark cycle, so that we feel awake during the day and sleepy at night. It gets the gut ready for food digestion during the day but helps us not to feel hungry when we are asleep at night. It determines when we are most alert (mid-morning), when we are most coordinated (early afternoon) and when we have the most muscle strength (late afternoon). Body temperature and blood pressure also increase and decrease throughout the day. Even our immune systems operate on a 24-h schedule, guided by the circadian rhythm.

Circadian rhythms are not unique to humans: almost every organism on Earth has a biological clock. Plants’ clocks prompt their leaves to open during the day and close at night. The clocks of nocturnal animals promote activity at night and sleep during the day. By tracking changes in the length of daylight, plants and animals can follow a yearly rhythm as well as a daily one. From flowers blooming in spring to Monarch butterflies migrating before winter, biological clocks are responsible. Except for in the darkest caves and deepest oceans, where sunlight never reaches, all life on our planet is in sync with the rotation of the Earth.

THE COGS OF THE CLOCK

Our biological clocks are unlike any clock that we could read. The cogs of the clocks are proteins. Clock proteins are produced and broken down in a cycle that lasts 24 h (see Box 1 for detailed explanation). This cycle ticks away in every cell in the body, meaning that each cell has its own clock. But how do all of these separate tiny clocks stay in

Box 1

Clock genes and the 2017 Nobel Prize.

PERIOD

The clock gene that codes for the PER protein.

PER

A protein involved in setting the circadian rhythm: its levels fluctuate in a regular 24-h cycle.

CYTOPLASM

The jelly-like substance that gives cells their shape.

In 1971, Seymour Benzer and Ronald Konopka found a strange fruit fly that had an altered circadian rhythm. The researchers discovered that this fly had a mutation in one gene, which they named **period** [1]. This was the first evidence that our clocks are controlled by our genes. On this day, the first “clock gene” was discovered.

So how does *period* make our clocks tick? Scientists found that *period* makes a protein called **PER**. PER is made and destroyed in a continuous 24-h cycle (Figure 2). During the night, *period* gives instructions for PER to be made. As PER builds up in the cell’s **cytoplasm**, it links up with another protein, TIM. When linked to TIM, PER can enter the cell’s nucleus—where the *period* gene lives. Here, PER tells *period* to stop making more PER. During the day, PER is slowly destroyed. As night approaches, the amount of PER in the cell is so low that the whole cycle begins again, and a fresh batch of PER is made. The discovery of this cycle was so monumental that 2017’s Nobel Prize went to the scientists who made it: Jeffrey C. Hall, Michael Rosbash, and Michael W. Young [2].

Box 1

SCN

Suprachiasmatic nucleus, which is the part of the brain that controls and synchronizes the whole body's circadian rhythm.

Figure 1

Aligning our clocks to sunlight. Sunlight is detected by special light-detecting cells, called ipRGCs, at the back of the eye. The ipRGCs send signals to the SCN in the brain. These signals are processed to coordinate the clocks within every cell in the body, so that they are synchronized with the light-dark cycle.

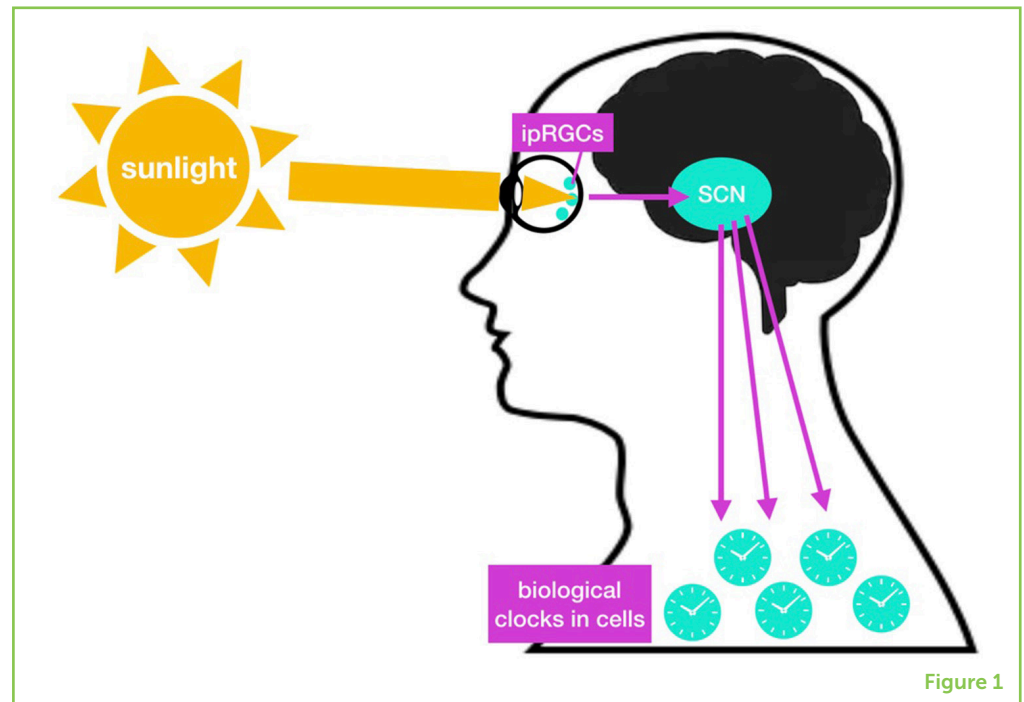
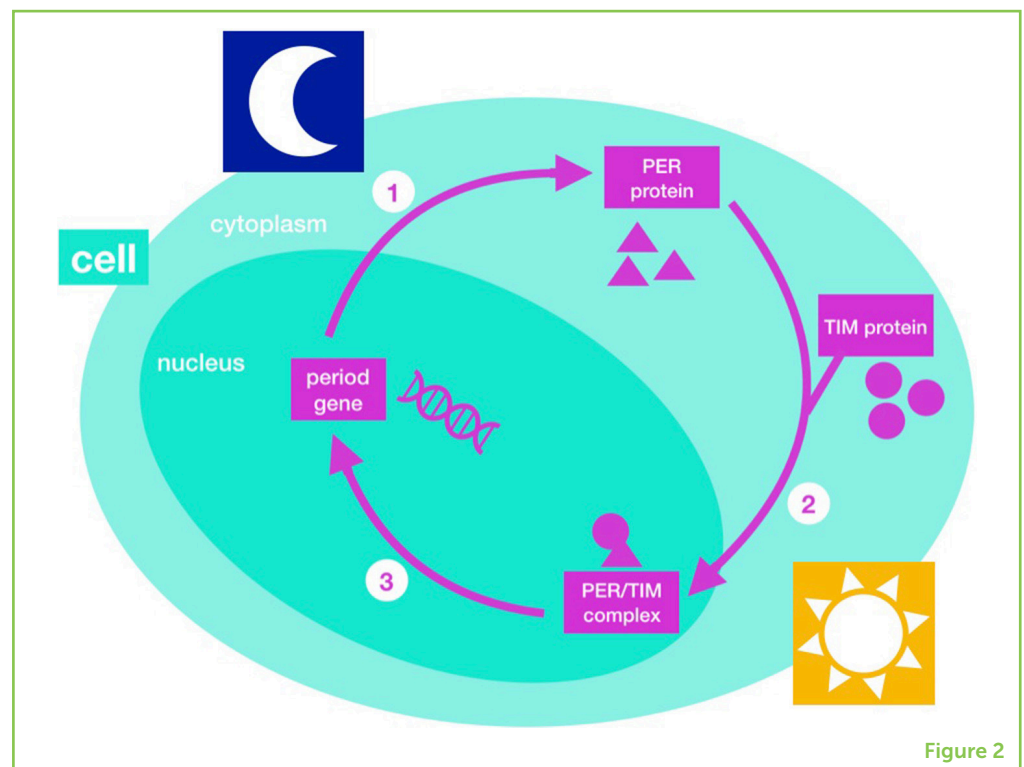


Figure 2

Cogs of the biological clock. The level of PER protein follows a 24-h cycle, increasing at night and decreasing during the day. **(1)** The PER protein is produced from the *period* gene at night. **(2)** In the cytoplasm, the PER protein pairs with the TIM protein, allowing it to enter the nucleus. **(3)** When inside the nucleus, PER inhibits its own production. When the level of PER falls below a certain amount, the production of PER increases again. The whole cycle takes 24 h.



ipRGC

Intrinsic photosensitive retinal ganglion cell, which is a special cell at the back of the eye that detects light and sends this information directly to the SCN.

SETTING THE CLOCKS BY THE LIGHT OF THE SUN

Just like an old clock, biological clocks must be adjusted to the correct time every day. Light is detected by cells at the back of our eyes, called photoreceptors. Most photoreceptors detect light so that we can see the world around us. But, in 2002, a new type of photoreceptor was discovered that sends signals directly to the SCN [3]. These special photoreceptors are called intrinsic photosensitive retinal ganglion cells, or **ipRGCs**. If the ipRGCs are working, even blind people can keep their rhythms aligned with the sunlight [4].

Using sunlight, the SCN can adjust the circadian rhythm to gradual changes in daylight hours as we progress through the seasons. But sudden changes in the light-dark cycle can leave us feeling totally out of whack. You may have experienced this yourself: it is called jet lag. Since the invention of airplanes, humans have been able to cross time zones in a matter of hours. An airplane can dump us in bright daylight when our biological clocks are preparing us for sleep. This can leave us feeling drowsy, dizzy and even queasy. Symptoms of jet lag can last for several days, because the SCN takes time to align itself with the new time zone. Now that you know that the SCN uses light to adjust to the time of day, you would not be surprised to hear of the best cure—spend some time in the sun!

ARE WE CONFUSING OUR CLOCKS?

For over four billion years, the sun was the sole source of light on planet Earth. Only 150 years ago, Thomas Edison invented the light bulb. Since then, our planet has been awash with light. We take our access to light for granted—it is as easy as the flick of a switch. However, should we flick the switch more cautiously? Research suggests that artificial light interferes with our circadian rhythms.

THE PLANET THAT NEVER SLEEPS

Artificial light means that we can extend daytime activities into the night. It creates a 24-h culture, with restaurants and shops open throughout the night. We can do almost any activity, from reading to driving, at any hour of the day. There are benefits to this. For example, access to healthcare at all times is a lifesaving reality. But what about the doctors and nurses who work through the night? People who work at night must switch their sleep-wake cycles back and forth, and often go days without seeing any natural sunlight. This can cause their biological clocks to get confused, and then all the things that depend on their clocks will also get confused, including sleep. The possible health

Box 2

The consequences of a confused circadian rhythm and sleep loss.

Proper sleep and a regular circadian rhythm are essential for keeping our bodies and minds functioning well. Which is more important—sleep or the circadian rhythm? This is a tough question to answer, because it is hard to disrupt one without disrupting the other. If you confuse your circadian rhythm (e.g., with jet lag), you will usually also lose some sleep. If you stay awake at night (e.g., because of night-time screen use), then this can disrupt your circadian rhythm. Short disruptions can cause immediate problems, which are usually reversible with a good night of sleep. Chronic sleep loss or circadian confusion can lead to long-term problems for the body and mind.

Short-term sleep loss or jet lag

- Trouble concentrating
- Increased stress
- Emotional distress
- Feeling unwell
- Memory problems and difficulty learning
- Poor physical performance and coordination

Long-term sleep loss or circadian confusion

- Mood disorders and psychological problems
- Heart and blood pressure issues
- Obesity and diabetes
- Reduced immune response
- Increased risk of cancer
- Worsening of existing medical conditions

Box 2

consequences of this are listed in Box 2. We should do all that we can to keep our circadian clocks in time.

SCREEN TIME

There is a newer enemy to our circadian rhythms: LED screens. Phones, computers and TVs have LED screens, which emit a huge amount of blue light. Blue is the color of light that ipRGCs are best at detecting. When this blue light comes from the sun it is a good thing—our brains get the signal from ipRGCs, “it is daytime, stay awake.” The SCN responds by inhibiting the production of a hormone that makes us sleepy, called melatonin. When the sun sets, there is no more natural blue light around, and so melatonin is produced, and we become sleepy (Figure 3).

Now imagine what happens if you turn on an LED screen after dark. Blue light will be detected by your ipRGCs, which cannot tell that the blue light is not from the sun. So, your brain gets the same signal, “it is daytime, stay awake.” The SCN tells the body to produce less melatonin and the level of melatonin falls [5]. With little melatonin around, it can be very difficult to fall asleep, even at bedtime. To avoid confusing our circadian clocks, we should try not to use electronic devices after dark; it may even be best to put them in a different room for the night. This may seem drastic, but just one night of sleep loss and circadian confusion can have serious effects on the body and mind (Box 2).

Figure 3

Effect of light on the sleepy hormone. Melatonin is a hormone that makes us feel sleepy. **(A)** Sunshine stops new melatonin being made (in picture, tap is OFF). But melatonin is always being broken down (in picture, dripping drain). So, in the daytime, the level of melatonin in the body is low, and we do not feel sleepy. **(B)** Darkness triggers the production of melatonin (in picture, tap is ON). So, the level of melatonin rises and we become sleepy when it is time for bed. **(C)** Using LED screens after dark interferes with this rhythm by stopping melatonin production, just like the sun does. This stops us from feeling sleepy even though our bodies are ready for bed.

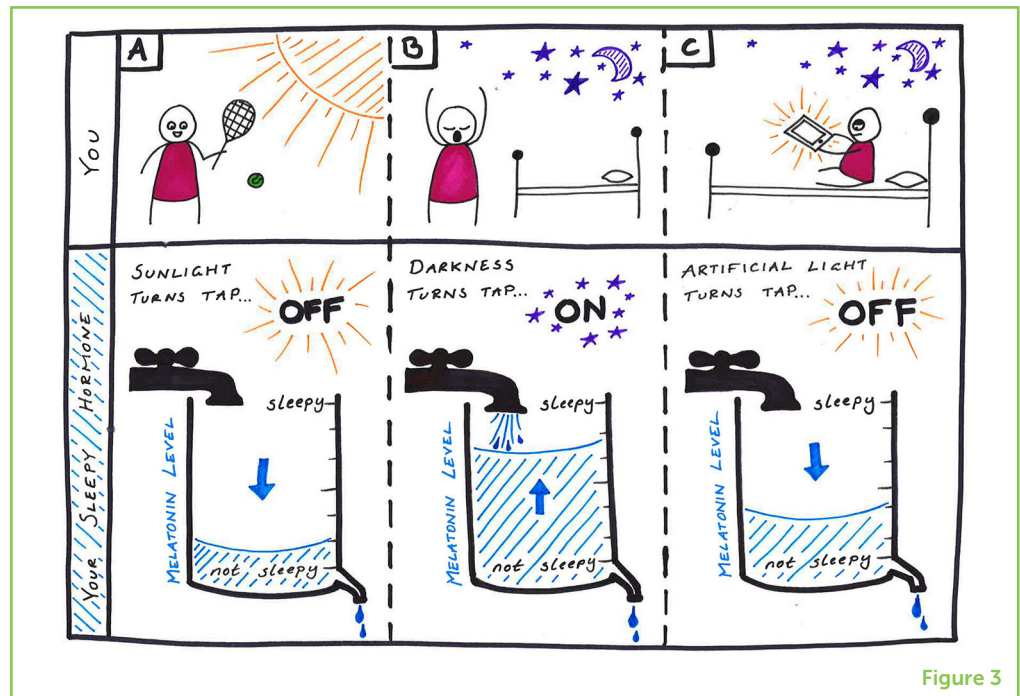


Figure 3

SUMMARY

Without us being able to see or read them, tiny clocks within our bodies keep time with the Earth's rotation. These clocks control the behavior of nearly all organisms on the planet, ensuring that we all do the right things at the right time of day. The cogs of these clocks are genes and proteins, cycling in a 24-h rhythm within every cell. These cellular clocks are all coordinated by a central, grandfather clock in the brain. Sunlight is used to keep the internal rhythm in sync with the world around us. Normally, this whole process happens so seamlessly that we are not even aware of our biological clocks. But when our clocks are out of sync, we feel the effects. Our modern world, with 24-h light, LED screens, and airplane travel, can confuse our biological clocks. We should do what we can to help our clocks to keep time.

AUTHOR CONTRIBUTIONS

KFA and JJH researched and wrote the article together.

ACKNOWLEDGMENTS

We would like to thank Isabell Whitely for her careful review of the article and Carles Bosch for his insightful comments on the figures. KA would also like to thank the Pathological Society for funding her placement with JH.

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SUBMITTED: 25 July 2018; **ACCEPTED:** 14 January 2019;

PUBLISHED ONLINE: 05 February 2019.

EDITED BY: Silvia A. Bunge, University of California, Berkeley, United States

CITATION: Addison KF and Harris JJ (2019) How Do Our Cells Tell Time? *Front. Young Minds* 7:5. doi: 10.3389/frym.2019.00005

CONFLICT OF INTEREST STATEMENT: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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YOUNG REVIEWERS

LAURI, AGE: 16

I live in Finland near to the sea. Music and sports are my hobbies.



**TUOMAS, AGE: 15**

I live in Finland.

AUTHORS**KATHARINE F. ADDISON**

I am entering the second year of my undergraduate degree at the University of Cambridge. I am fascinated by the workings of the brain. This summer, I am pursuing my interests in the Neurophysiology Department at the Francis Crick Institute in London. I hope to specialize in Neuroscience for my degree and continue my studies to Ph.D. level. I am particularly interested in the clinical applications of the science, such as treatments for Alzheimer's disease and treatments for sleep disorders.

JULIA JADE HARRIS

I am interested in how the brain has evolved so that it can use very little energy to do complicated tasks, and whether sleep is important for the brain to stay energy efficient while also learning new things. To investigate these topics, I measure the brain activity of mice while they learn tasks and while they sleep. I carry out my research between Imperial College London and the Francis Crick Institute. I received my undergraduate degree from the University of Oxford and did my Ph.D. at UCL.

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DAILY RHYTHMS OF THE BODY AND THE BIOLOGICAL CLOCK

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YOUNG REVIEWER:



ORI

AGE: 12

Earth's rotation creates a cycle of day and night, which is observed as changes in light levels and temperature. During evolution, plants and animals adapted to these cycles, developing daily cycles of physical and behavioral processes that are driven by a central biological clock, also known as the circadian clock. Even in the absence of changes in light between day and night, the biological clock creates cycles called circadian rhythms. The nervous system transfers information about the external light level to the biological clock in the brain, which matches the clock's cycle to the external environment. The biological clock prepares the body for environmental changes. The modern world has created disruptions in the circadian clock's timing, because of electrical lighting, flights to other time zones, and work during the night. The study of chronobiology studies the mechanisms of the biological clock and the clock's influence on human health.

INTRODUCTION

Repeating processes, such as waves moving up and down, create a rhythm characterized by a consistent cycle. The earth's rotation creates the phenomenon of day and night in a 24-h cycle. This cycle results in environmental changes during the day, such as higher light levels and warmer temperatures. So, it is not surprising that, during evolution, the daily cycle was a significant factor to which animals and plants adapted. Many processes in our bodies show daily fluctuations, including our body temperature, blood pressure, and hormone levels. For example, the secretion of a hormone called melatonin (the sleep hormone) reaches its peak late at night and decreases in the morning, whereas, in the morning, the hormone cortisol reaches its peak. The concentrations of many other proteins in our bodies also show daily fluctuations. We are also all aware of daily cycles in our emotional and behavioral processes, such as our alertness and our ability to concentrate or learn, and the cycle of wakefulness and activity during the day and sleep during the night.

THE BIOLOGICAL CLOCK CREATES DAILY RHYTHMS

What drives the daily rhythms in our bodies? One possibility is that the body responds to cyclical changes in the environment. An increase in light levels with sunrise makes us wake up, and the darkness at night results in an increase in melatonin, which promotes sleep. An additional explanation is that there is an internal mechanism in the body, creating the daily rhythm independently of environmental changes. How can we differentiate between these two mechanisms? In 1962, a French scientist named Michel Siffre conducted an experiment on himself. He lived for 2 months in a cave in the Alps, without exposure to daylight, with constant temperature, and without knowing if it was day or night. He lived in a tent with an artificial lighting, connected to machines that tracked his body's activity. The results of the experiment (Figure 1) showed a daily, cyclical, organized activity pattern, where the significant difference was that each day he woke up about half an hour later. In fact, the length of the "day" he lived by in the cave was 24.5 h. The main conclusion was that the body has an internal clock, which is independent of the environment's fluctuations. This clock creates daily rhythms, with a cycle slightly longer than 24 h, even in the absence of environmental cues. In normal conditions, when we are exposed to sunlight, our clock cycle shortens to exactly 24 h.

Siffre's experiment earned him the nickname "the caveman," and received much publicity. But scientists who conducted similar experiments in animals and plants already knew about the existence of a biological clock and called it the **circadian clock**. In Greek, "circa" means "about" and "diem" means "day." The circadian clock exists in almost all animals on earth—in mammals, insects, plants, fungi, and

CIRCADIAN CLOCK

A biological system that generate rhythmic changes in physiological and behavioral functions that repeat themselves every 24-h. The system is based on a network of proteins interacting with each other within a cell, as well as interaction between different cells. The central clock resides in the Suprachiasmatic nucleus in the brain. Examples of circadian rhythms that are regulated by the clock include the sleep/wake cycle, core body temperature, and melatonin secretion. The circadian clock is entrained to the environment by the 24-h changes in light exposure.

Figure 1

Siffre's cave experiment. The daily activity from the beginning of the experiment (top) to the end (bottom). The thick lines symbolize the time Siffre spent asleep. The first 10 days (1–10) and last 10 days (35–45) were spent in natural conditions outside the cave, and therefore his activity was synchronized to a 24-h clock. While in the cave, his activity reflects the cycle of the circadian clock, which is about 24.5 h, which is why his sleeping time can be seen to shift to the right.

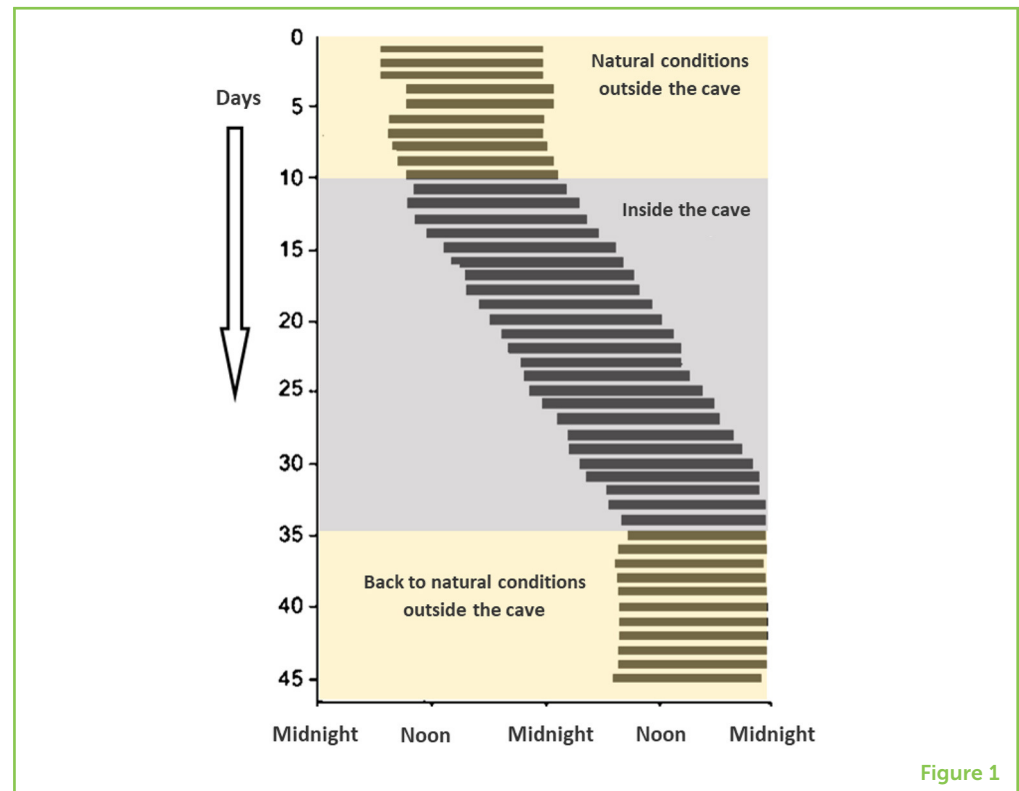


Figure 1

even bacteria. The cycle of the clock is different in different creatures, and even among individuals from the same species, and can be shorter or longer than 24 h.

PERIPHERAL CLOCKS

These clocks are in cells, tissues, and organs across the body. They receive information from the central clock in the brain and from other internal and external sources. For example, mealtimes are cues for peripheral clocks in the liver, kidney, and pancreas. The relationship between central and peripheral clocks is like the relationship between a conductor and musicians in an orchestra.

The ability to create daily rhythms exists in different cells, tissues, and organs in the body. These clocks, called **peripheral clocks**, are obedient to the central clock, which is located at the base of the brain in an area called the **suprachiasmatic nucleus (SCN)**. This small region is the size of a rice grain and includes about 20,000 nerve cells. In experiments with mice in which the SCN is surgically removed, the behavior of the mice is quite normal, except that they lose the ability to keep their daily rhythms under constant conditions.

WHY DO WE NEED THE CIRCADIAN CLOCK?

We assume that the circadian clock exists in so many creatures because it provides some advantage to the survival of those species. To understand what this evolutionary advantage is, experiments were conducted on animals with faulty circadian clocks, both in the lab and the natural environment. In laboratory light-darkness conditions, animals without circadian clocks will still exhibit daily rhythms. For example, in lab conditions in which there is no danger of death from predators, fruit-flies with defective biological clocks have similar lifespan as flies with intact clocks.

SUPRACHIASMATIC NUCLEUS (SCN)

A small brain structure that consists of around 20,000 nerve cells and function as the central clock. The SCN is located in the hypothalamus, above the area where the optic nerves from the eyes cross.

NEGATIVE FEEDBACK LOOP

A process that paces itself. The thermostat is an example of negative feedback; when the temperature rises to a certain value, the thermostat turns off the heat. When the temperature goes down, the heating starts again. This process creates upward and downward temperature swings.

SYNCHRONIZE

Adjusting two waves to each other, so peaks and troughs coincide or present at a fixed time difference (synchronization is possible only between waves that have the same cycle length).

The advantage of the circadian clock becomes clear when examining animals in natural conditions, in competition with their own kind. For example, an experiment done on chipmunks demonstrated that, if the SCN was surgically removed, these rodents showed decreased survival in the forest, since their activity patterns were irregular and predators found them more easily [1]. Another experiment was conducted with a mix of two different species of bacteria, one with a short daily cycle (23 h) and the other with a long cycle (30 h) exposed to short and long days [2]. The results showed that one species pushed the other one aside. The “winning” species was the one whose circadian rhythm better suited the day’s duration, so the species with the long cycle took over the culture in long-day conditions, while the species with the short cycle took over the culture that was grown in short-day conditions. These studies and others show that the circadian clock allows the body to act in harmony with the external environment.

THE CLOCK’S GENETICS

The first gene of the circadian clock was discovered in 1971, through research on a tiny fly called *Drosophila*, which is commonly used by genetic researchers [3]. The researchers gave the flies a chemical that damaged the genes in their DNA. Then they observed the daily activity of the flies and searched for those whose cyclical activity was disrupted. They soon found a fly in which the sleep and wakefulness times changed each day. This fly had lost its circadian rhythm because of one damaged gene, which got the name *period* (*per* for short). *Per* is a gene found in all animals, including humans. Later, the *Clock* gene was discovered (*Clk* for short) in mice. Over time, additional genes involved with the circadian clock were discovered.

The genes in animals are different from those in plants or fungi, but the principle of operation is similar, and is an example of a **negative feedback loop**. In this loop (Figure 2), the CLK protein stimulates the production of the PER protein. When the PER protein reaches a high level, it delays the production of the CLK protein. This delay results in a gradual reduction in the PER protein. The relationship between these two proteins leads to their daily fluctuations: when PER is high, CLK is low, and vice versa. These findings won three American scientists the Nobel Prize in physiology or medicine in 2017, for their studies using *Drosophila*.

THE INFLUENCE OF LIGHT ON THE BIOLOGICAL CLOCK

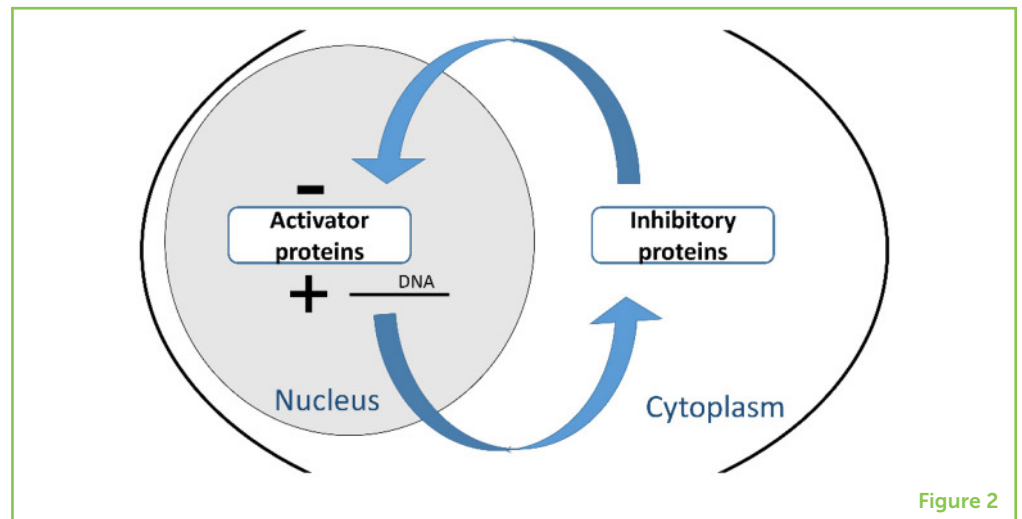
As Siffre discovered in his cave experiment, the circadian clock operates even without exposure to cycles of light and darkness, although the daily cycles are longer than 24 h. In a natural environment, natural light is a cue that **synchronizes** us to a 24-h clock. Additional time clues include temperature and social time cues,

Figure 2

The molecular circuit of the clock. Activator proteins (such as CLK) in the cell nucleus increase the production of clock proteins, which are inhibitory (such as PER). The inhibitory proteins move back to the nucleus where they inhibit the activator proteins, slowing down their own production. When the level of the inhibitory proteins goes down, the inhibition stops and a new cycle resumes. This is an example of a negative feedback loop.

INTRINSICALLY PHOTSENSITIVE RETINAL GANGLION CELLS (IPRGC)

A type of nerve cells in the retinas of mammals, which contain light receptors that do not participate in the process of seeing, but rather in the synchronizing of the circadian clock to light from the environment.



such as mealtimes, work times, and study times. But light is considered the strongest time cue influencing the circadian clock.

How does this happen? In the retina of the eye, there are three types of molecules that transform light energy to the electrical activity that travels to the brain. Two types of receptors, the rods and cones, are used for seeing. A third, lesser-known group of receptors is called **intrinsically photosensitive retinal ganglion cells** (ipRGCs). These receptors supply information to the nerve cells that connect the retina to the SCN. Two decades ago, researchers found that the ipRGCs contain a light-sensitive pigment called melanopsin, and they figured out how melanopsin helps to synchronize the circadian rhythms with the external environment [4].

THE INFLUENCE OF MODERN LIFE ON THE BIOLOGICAL CLOCK

Shortly before the identification of melanopsin, researchers discovered that the light-detecting molecules that influence the circadian clock are sensitive to blue light, which is light with a wavelength of 460 nanometers. This finding has great significance for the modern world, because today we are exposed not only to sunlight, but to electronic light sources that we use long after sunset. LED bulbs and devices, such as televisions, computers, and smartphones all produce blue light, therefore influencing our circadian rhythms.

There are other ways that modern life makes it harder for our circadian clocks to synchronize with the environment. A common example is flying to far-away countries, in which case the circadian clock must be delayed or brought forward by a few hours in order to synchronize. This process can take a few days and it is experienced as unpleasant sensations called jet lag. Jet lag can be caused by shifting the light cycle by just a few hours (Figure 3). Studies show that people frequently

Figure 3

Jet lag experiment. An example of the activity of a hamster (nocturnal animal). The gray background symbolizes hours of darkness, and the yellow background symbolizes hours of light. After 8 days (top) the light is switched off 6 h earlier (indicated by the arrow). The hamster needs 1 week to synchronize to the new rhythm. The 6-h shift in the light-darkness cycle is equivalent to the jet lag experienced after flying east, for example from Israel to Japan, where bedtime comes earlier.

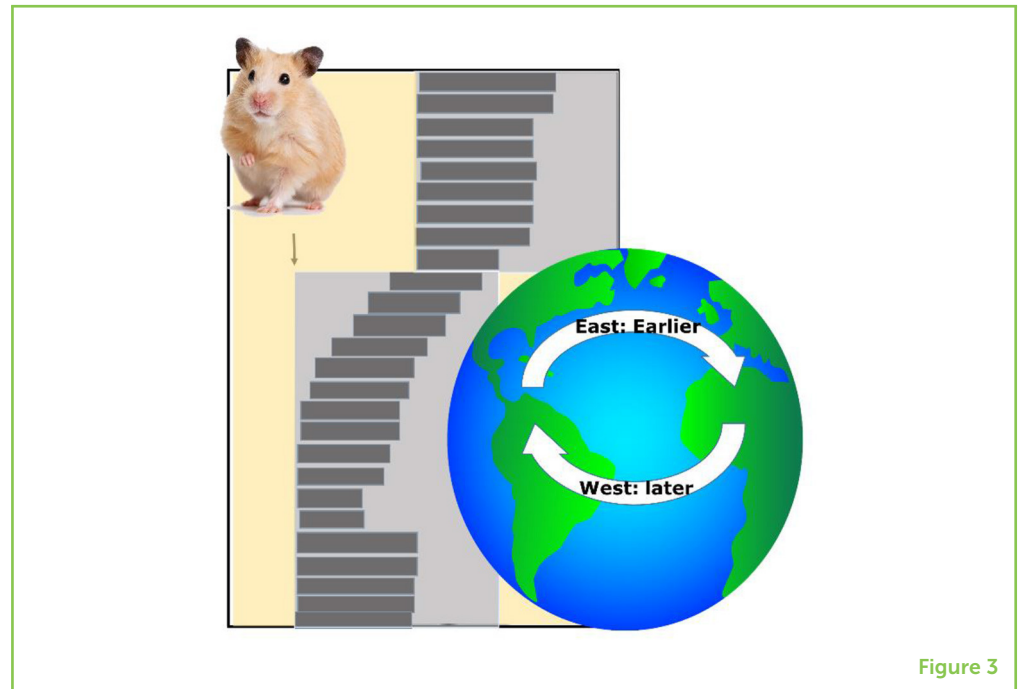


Figure 3

experiencing jet lag are at higher risk of cancer and other chronic illnesses. Higher levels of certain diseases/disorders are also seen in people who work at night, who are effectively experiencing prolonged social jet lag. To reduce the health damage that can result from these disruptions to the circadian rhythm, it is recommended that we are exposed to daylight as much as possible, and that we avoid the light from our screens at night.

SUMMARY

The circadian clock is built from genes and nerve cells that allow us to be in complete coordination with the daily fluctuations of the environment. Exposure to artificial light makes it harder for the circadian clock to synchronize with the environment, which could lead to health issues. The science of **chronobiology** (biological clock research) focuses on understanding the circadian clock's mechanisms and the differences in clocks between people. This knowledge will help scientists to develop personalized medicine in the future, which will consider the unique body rhythms of each and every one of us.

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CHRONOBIOLOGY

The scientific discipline that studies biological timing systems and their effects on health and functioning.

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SUBMITTED: 23 December 2020; **ACCEPTED:** 11 March 2021;

PUBLISHED ONLINE: 20 April 2021.

EDITED BY: Idan Segev, Hebrew University of Jerusalem, Israel

CITATION: Shochat T and Tauber E (2021) Daily Rhythms of the Body and the Biological Clock. *Front. Young Minds* 9:645707. doi: 10.3389/frym.2021.645707

CONFLICT OF INTEREST: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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YOUNG REVIEWER

ORI, AGE: 12

My name is Ori and my favorite food is chopped Gruffalo. I spend most of my time at school. I like to program games and websites, design logos, edit videos, play the piano, and play on the computer. I participate in the program for talented youth in mathematics at Bar-Ilan University.



AUTHORS

TAMAR SHOCHAT

Tamar Shochat studies factors involved in sleep regulation as well as health and functional outcomes associated with human sleep. She studies mostly non-clinical populations that are particularly vulnerable to sleep disruption, such as adolescents, older adults, and shift workers, in their ecological surroundings. She is particularly interested in studying the consequences of mistimed sleep due to the conflict between the circadian clock and social constraints, also known as circadian misalignment or social jet-lag. This conflict may be due to evening light exposure, delayed sleep phase (evening types), and shift work.



**ERAN TAUBER**

I am a scientist interested in the genetics of biological clocks and how changes in these genes allow the clock to function under different environmental conditions. We are also researching what genetic basis causes animals to be active at different times of the day. I head the laboratory for biological clocks at the University of Haifa and our main research animal is the fruit fly. *etauber@univ.haifa.ac.il



THE SCIENCE OF DREAMS

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Department of Psychological and Brain Sciences, University of Massachusetts Amherst, Amherst, MA, United States

YOUNG REVIEWERS:

EXPLORA
SCIENCE
CENTER AND
CHILDREN'S
MUSEUM



AGES: 8–14

STEM GIRL
AMBASSADORS



AGES: 10–12

Dreams are a common experience. Some are scary, some are funny. Recent research into how the brain works helps us understand why we dream. Strange combinations of ideas in our dreams may make us more creative and give us ideas that help us to solve problems. Or, when memories from the day are repeated in the brain during sleep, memories may get stronger. Dreams may also improve our moods. Together, these studies show that dreams and sleep are important for performing well when we are awake.

When she was 8, my daughter told me about one of her dreams. She was in a spaceship with some animals. Although she knew she was in a spaceship in her dream, when telling me about the dream, she realized the spaceship was actually a washing machine. At times, she and the animals would be out in space, but they also came back to earth. She told me the dream with a laugh and then moved on with her day, ignoring the crazy animals and spaceships that entertained her in her sleep.

Since we remember our dreams and then often forget them, what is their purpose? Why do we dream about the things we do? New

research tools, particularly those that can be used to investigate the brain, are being used to answer these questions.

WHAT ARE DREAMS?

Although it is hard to define what a dream is, for the purpose of this article, we will define dreams as our thoughts during sleep that we recall when we wake up. So, sleeping dreams are not the same as “daydreaming.” Dreams are mostly visual (made up of scenes and faces; sound, taste, and smell are rare in dreams [1]). Dreams can range from truly strange to rather boring, snapshots from a recent event.

To study dreams, scientists need a measure of dreaming. Most studies use dream reports (a person writes out her dreams when she wakes up) or questionnaires (a person answers questions like “How many dreams have you recalled in the past month?” [2]). Dreams are more likely to be recalled when a person is woken up from REM sleep. REM sleep is a type of sleep that is named for the **rapid eye movements** that can be measured during this stage of sleep. We do not dream as much in non-REM sleep, the sleep stages that make up the rest of the night, and dream reports from non-REM sleep are often less strange.

Dream frequency (how often dreams happen) and content (what dreams are about) is very different for everyone, and there are many reasons why this may be true. For example, you will remember dreams more if you are woken up by someone or by an alarm clock. This might be because you can still recall that dream memory while it is fresh but, if you wake up on your own, you will transition through a few sleep stages and possibly lose that dream memory. Dream recall changes with age, too. Older people are less likely to report dreaming. This could also be related to memory: since older people have weaker memories, it could be that they dream but cannot remember their dreams by the time they wake up. A brain area called the **medial prefrontal cortex** is also related to dream recall. If this brain area is damaged, the person recalls few dreams, which may mean the person dreams less (or not at all). Also, how tightly packed the brain cells are in the medial prefrontal cortex can vary from person to person, which may cause some healthy people to dream more or less than other healthy people. There are also genes that affect how much REM sleep people get. People with less REM sleep may not have the strange dreams that tend to come in REM. So, how long you sleep, your age, and your genetics may all explain why you dream more or less than someone else.

Do dreams actually happen while we sleep, or are they ideas that come to us when we wake up and we just “feel” like it happened during sleep? A recent study using a type of brain imaging called **magnetic resonance imaging** or (MRI: Read more in the Young Minds article “How Is Magnetic Resonance Imaging Used to Learn About

RAPID EYE MOVEMENT (REM)

A stage of sleep in which the eyes move rapidly and there is no muscle activity.

MEDIAL PREFRONTAL CORTEX

A specific area in the front of the brain that is associated with dream recall but also has a role in memory and decision-making.

MAGNETIC RESONANCE IMAGING (MRI)

A tool used to take pictures of internal body parts (including the brain). MRI can also be used to measure the activity in the brain.

Figure 1

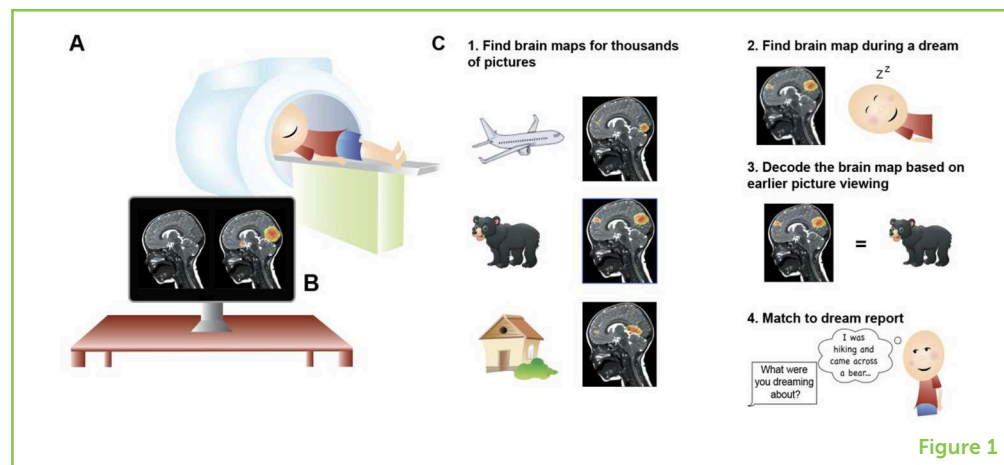
(A) Magnetic resonance imaging (MRI) is a way to investigate the brain. The person lies on a bed inside a giant magnet. (B) MRI can measure the structure of the brain and the areas of the brain that are active. (C) MRI was used to measure dreaming. First, while the participant was awake, they viewed thousands of pictures in the MRI. This told scientists the specific brain responses to specific pictures. Later, when the participant slept in the MRI, scientists measured the brain activity patterns and matched this to the brain responses to the pictures the participant saw when they were awake. Scientists guessed that the best match would tell them what the participant was dreaming about. By asking the participant about their dreams in the MRI, scientists found that the dreams did tend to match the pictures predicted by the brain activity.

HIPPOCAMPUS

An area in the brain that is thought to be important for short-term memory.

NEURON

A cell in the nervous system (brain and spinal cord) that can transmit information to other cells.

**Figure 1**

the Brain?" [3]) helped answer this question (Figure 1A). The scientists made maps of the brain activity that occurred when people looked at pictures of things—keys, beds, airplanes. Later, the people in the study slept in the MRI machine. The scientists matched the pattern of brain activity from the people as they slept to brain activity patterns for the pictures they viewed earlier, and then chose the best match (Figures 1B,C). This match predicted what the person said they dreamed about 60% of the time. Although 60% is not perfect, it is better than guessing! [4]. This means that dreams are created in the brain during sleep.

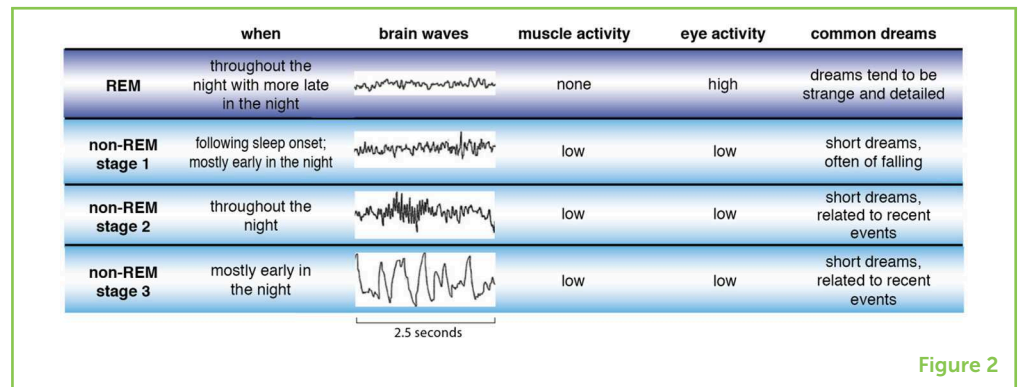
DREAMS SUPPORT MEMORIES

What is the purpose of our dreams? Researchers have found that sleep is important for memory (see this *Frontiers for Young Minds* article; "Thanks for the Memories..." [5]). Memories move from temporary storage in the **hippocampus**, a brain structure that is very important for short-term memory, to permanent storage in other parts of the brain. This makes the memories easier to remember later. Memories improve with sleep because the memories are replayed during sleep [6]. If you want to learn all the words to your favorite scene in a movie, you might re-watch that scene over and over again. The brain works the same way: **neurons** (brain cells) that are active with learning are active again and replay the learned material during sleep. This helps store the memory more permanently.

Memory replay may show up in our dreams. Dreams in non-REM sleep, when most memory replay happens, often contain normal people and objects from recent events. However, sleep switches between non-REM and REM sleep (see Figure 2). So, bizarre dreams in REM sleep may come from a combination of many different recent memories, which were replayed in non-REM sleep, and get jumbled up during REM sleep. If dreams help with memory processing, does that mean your memories are not being processed if you do

Figure 2

There are four types of sleep—REM sleep (purple) and three stages of non-REM sleep (blue). REM stands for rapid eye movements, which happen during this stage of sleep. During REM sleep, muscle and brain activity also differ from other sleep stages. Characteristics of dreams tend to be different for each of these sleep stages.



not dream? No. Memories are moving to storage even if we do not dream.

DREAMS IMPROVE CREATIVITY AND PROBLEM SOLVING

My daughter's dream of a spaceship made a great story that she recited to me, and later, to her classmates. The images were intense and interesting, inspiring her to draw scenes in a notebook and write about the dream for school. This is an example of how dreams can help make us more creative. Mary Shelley, the author of the book *Frankenstein*, got the idea for her book from a dream. Even scientists get ideas from dreams [7].

To measure creative problem solving, scientists used a remote associates task, in which three unrelated words are shown, and the person is to come up with a word they have in common. For instance, HEART, SIXTEEN, and COOKIES seem unrelated until you realize they all are related to SWEET (sweetheart, sweet sixteen, and cookies are sweet) (Figure 3). The scientists wanted to see whether sleep helped people do better on this task. They found that people were better at thinking of the remote solution if they had a nap, particularly a nap with REM sleep. Given that REM is when most bizarre dreaming occurs, this supports the idea that these dreams might help us find creative solutions to problems [8].

This study and research like it gives us reason to believe that REM dreams may help us be more creative and solve problems. Many different memories may be activated at the same time and when these memories are mixed together, the result when we wake up may be both the memory of a strange dream and a unique perspective on problems.

DREAMS REGULATE OUR MOODS AND EMOTIONS

Dreams are usually emotional. One study found that most dreams are scary, angry, or sad.

Figure 3

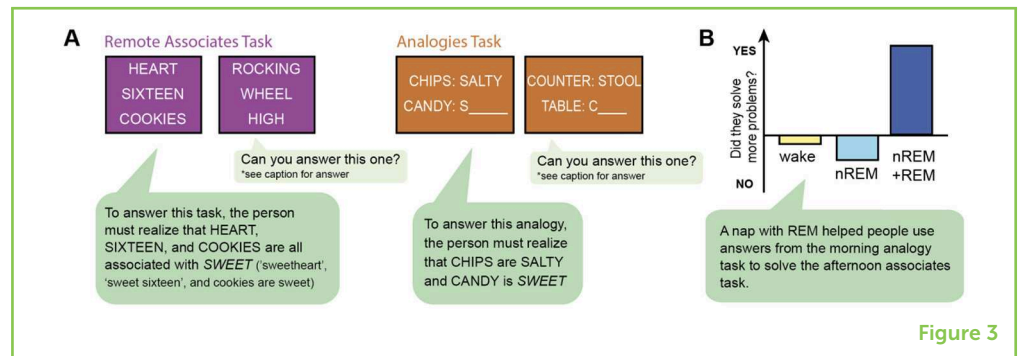
REM sleep helps people find creative solutions. In the morning, participants did two tasks to test creativity and problem solving (A). They did one task again in the afternoon. In between, they either stayed awake ("wake" group) or took a nap. Those that took naps either did not have REM sleep in their nap ("nREM" group) or had both nREM and REM sleep ("nREM + REM" group). (B) If subjects stayed awake between the morning and afternoon tests (yellow bar), they did not improve on the task. They also did not improve if they had a nap that was only nREM sleep (light blue bar). But, if they had a nap with both nREM and REM sleep, they did better in the afternoon compared with when they did the task in the morning (dark blue bar). So, REM sleep must help us find creative solutions (from Cai et al. [8]).

AMYGDALA

An area of the brain involved in the experience of emotions.

THREAT SIMULATION THEORY

A theory of dreaming that says that threats (things that could be bad) are simulated or practiced in your dreams to prepare you for those situations when you are awake.

**Figure 3**

Dreams might seem to be emotional simply because we tend to remember emotional things better than non-emotional things. For example, in waking life, the day you got a puppy is more memorable than a normal school day. So, dreams about emotional events might be remembered more easily than boring, non-emotional dreams. It is also possible that dreams are emotional because one job of dreams is to help us process emotions from our day [9]. This may be why the **amygdala**, an area of the brain that responds to emotions when we are awake, is active during REM sleep. If you had a sad day, you are more likely to have sad dreams. But, sleep also improves mood—sleep after a disagreement or sad event will make you happier.

Dreams could also help prepare us for emotional events, through something called **threat simulation theory** [10]. For example, when I dreamt that my young daughter, who could not swim, fell into a swimming pool, recall of that dream convinced me to sign her up for swim lessons. By simulating this fearful situation, I could prevent it by being prepared.

These studies show us that sleep and dreams are important for our emotions. By processing emotions in sleep, we may be better prepared and in a better mood the next day.

CONCLUSIONS

There are different ways scientists measure dreams—from asking questions to using MRI. These studies show us that activity in the brain while we sleep gives us the interesting dreams we recall when we wake up. These dreams help us remember things, be more creative, and process our emotions.

We know most kids do not get enough sleep. Some diseases (like Alzheimer's disease) also make people sleep less, while others (like REM sleep behavior disorder and mood disorders) affect dreams directly. It is important to study sleep and dreams to understand what happens when we do not get enough sleep and how we can treat people with these diseases.

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SUBMITTED: 30 April 2019; **ACCEPTED:** 22 November 2019;

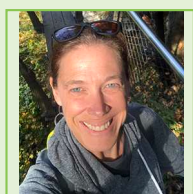
PUBLISHED ONLINE: 18 December 2019.

EDITED BY: Kathleen Y. Haaland, University of New Mexico, United States

CITATION: Spencer RMC (2019) The Science of Dreams. *Front. Young Minds* 7:140. doi: 10.3389/frym.2019.00140

CONFLICT OF INTEREST: The author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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YOUNG REVIEWERS

EXPLORA SCIENCE CENTER AND CHILDREN'S MUSEUM, AGES: 8–14

The Explora Young Minds reviewers are a group of science enthusiasts working with museum educators and mentors from the University of New Mexico. We enjoy learning about the brain through the articles. We also enjoy asking questions and making suggestions to help the scientists make their work more understandable for everyone! We were helped by our Science Mentor, Crina Floruta, who is a M.D./Ph.D. candidate working in a neuroscience lab and who is hoping to pursue a Neurosurgical residency in the future. She loves Albuquerque, hiking, reading, and talking about the brain with people.

STEM GIRL AMBASSADORS, AGES: 10–12

As a group of Ambassadors for STEM we are determined to help everyone around us realize how the skills of STEM are part of every day life. We come from many different schools to work together to encourage girls of all ages think outside the box, to challenge themselves in their learning, to seek support and encouragement from role models and be a strong voice.

AUTHOR

REBECCA M. C. SPENCER

I study human neuroscience at the University of Massachusetts, Amherst. I have a Ph.D. in Neuroscience from Purdue University and I did my post-doctoral training at the University of California at Berkeley. What interests me most is the question, "Why do we sleep?" To answer this, we study everything from naps in preschoolers to the sleeping brains of adults. My hobbies are trail running, playing with my kids, and inspiring young girls to be scientists. *rspencer@umass.edu



Scientific significance of sleep talking

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Reviewed by:



Empress
8 years old



Maya
10 years old



Mika
12 years old

Did one of your parents, siblings, or friends ever tell you that you were talking in your sleep? Nothing to be ashamed of! A recent study found that more than half of all people have had the experience of speaking out loud while being asleep [1]. This might even be underestimated, because often people do not notice that they are sleep talking, unless somebody wakes them up or tells them the next day. Most **neuroscientists, linguists**, and psychologists studying language are interested in our language production and language comprehension skills during the day. In this study, we will explore what is known about the production of overt speech during the night. We suggest that the study of sleep talking may be just as interesting and informative as the study of wakeful speech.

WHAT IS SLEEP TALKING?

Sleep talking (or *somniloquy*) can be considered as a part of a larger family of types of “sleep utterances,” such as mumbling, laughing, groaning, and whistling during sleep. The ancient Greek philosopher Heraclitus of Ephesus already observed someone sleep talking about 2,500 years ago, so it is not a very recent discovery. It happens at all ages (provided that one is capable of speaking!) and may occur during all parts of the night. Sleep talking is said to be more common in children than in adults. However, it might also be the case that sleeping kids are simply more often overheard (for instance, by their parents) than adults. Sometimes, sleep talking is placed among involuntary

behaviors that may happen during sleep (called “parasomnias”), such as sleepwalking, teeth grinding, and even types of sleep behavior disorders in which patients may injure themselves or their bed partner when involuntarily making dangerous movements during sleep. However, sleep talking is often very innocent and generally does not require any treatment. An exception is the sleep talking that may start to occur after a traumatic experience, as in the case of soldiers who fought in a war.

WHEN DO WE SLEEP TALK?

Human sleep consists of different stages (see the article *Why sleep?* by Manoach and Stickgold for

a nice overview) which can be distinguished by inspecting the recordings of electrical activity from sensors placed on someone's scalp, a method called **electroencephalography** (EEG; see Figure 1). While dreams can occur during all sleep stages, we are dreaming most vividly in a sleep stage known as “REM sleep” because of the occurrence of *Rapid Eye Movements*. During REM sleep, all body muscles (with the exception of the eye muscles, obviously) are paralyzed by neural structures in the brain stem, which prevent us from acting out our dreams. Accordingly, complex movements like sleepwalking normally occur only during non-REM sleep stages. In such cases, a small part of the brain appears to be awake while the rest of the brain is asleep [2]. This seems to be true for sleep talking as well: producing speech requires the planning and execution of rapid sequences of muscle movements, hence it will most likely occur in non-paralyzed, non-REM sleep stages [3]. This suggests that the speech we say out loud while sleeping (“sleep talk”) is not necessarily just the overt counterpart of the things we may silently say in our dreams or nightmares (“dream speech”). However, overt sleep talking during REM sleep has also been reported – which might happen when the brain stem briefly fails to paralyze the body muscles [4]. Anyway, the existence of sleep talking and of dreams shows that our brain is not completely “switched off” during sleep.

WHAT DO PEOPLE SAY DURING SLEEP?

The popular view, as encountered in pop songs and novels, is that people sometimes betray their innermost secrets during sleep because they have no

control over what they say. A nice example is the song *Nightmares* by Josh Ritter. Research has shown that the disclosure of personal secrets during sleep is very rare and uncommon [5], although it is not unusual to allude in sleep talk to things and people encountered during the day. Sleep talking may reflect someone's feelings, but not necessarily any “secret” feelings. Let's have a look at what people actually say while sleep talking and compare this to the wakeful speech we produce during the day. Here are some examples of sleep talk, taken from a large database [5]:

Example A: “Mm, hm – yes, yes”

Example B: “Peacock tree?! There's a tree full of peacocks and swallows and other colorations, absolutely, absolutely g-o-o-or-geous – get my camera, Larry, and don't forget to turn the film or I'll have fits when it gets back – come *on!* God! – you should *see* it.” [This was uttered with an air of brisk alert enthusiasm.]

Example C: “I wanna take a net – a note – a note”

At first sight, these utterances do not look that different from the things we say during the day. And indeed, in linguistic terms, the similarities between sleep talk and wakeful speech are striking. Utterances can be very simple and short such as in Example A, which is not very different from a short backchannel response in an everyday conversation. Example B, on the other hand, shows how complex sleep talk can

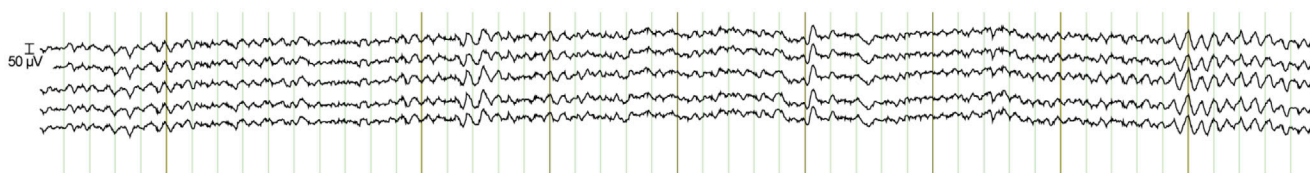


FIGURE 1 - Electrical brain activity as recorded by five electrodes placed on someone's scalp, measured in microvolts (μV). Small deflections in the waves depicted here show that this person is becoming a bit sleepy. Similarly, the inspection of such waves while someone is sleeping allows us to distinguish different sleep stages.

be. It includes different types of speech act including a question, a description of a visual scene, and an imperative (“get my camera”) directed at a specific addressee (“Larry”), with varying intonation patterns. Such speech production abilities during the night, as reflected in the above examples, suggest that brain networks involved in speech production may become activated while a person is asleep. Based on research of awake participants, we know that these networks reside for the greater part in the **frontal** and **temporal** lobes of the brain, mainly in the left **hemisphere**.

Like everyday colloquial speech, sleep talk may contain speech errors. Example C shows a putative speech error that is immediately corrected by the sleeping speaker. Problems in word finding and in the correct encoding of sounds that make up a word seem a bit more common in sleep talk than in everyday speech. Sometimes, they even resemble the word finding difficulties of people suffering from specific types of aphasia, a language disorder that is caused by dysfunction of (parts of) the brain. Another characteristic of some instances of sleep talk is the apparent lack of thematic coherence of subsequent utterances. One possibility is that such utterances are related to dream content, in which thematically different and apparently unrelated scenes may rapidly follow one another. In contrast with such decreased abilities during sleep, there are some anecdotal reports of people being more creative or eloquent in sleep talk than in wakeful speech, for instance when speaking a second language. Another important difference between sleep talk and everyday speech is that people often do not remember the next day that they have overtly produced speech in their sleep, let alone what they have said while sleeping.

In contrast to word finding problems and incidental lack of coherence, the grammatical structure of sleep-talk sentences is often perfectly correct. Apparently, our brains are capable of producing grammatically correct sentences while we are asleep. This suggests that building the grammatical structure of a sentence in speech production (including wakeful speech) is

a largely automatic process, which may take place without the need for a speaker to pay too much attention to it. In turn, this allows the speaker to focus more on the content of the message [6]. This is one example of how the study of sleep talk can have implications for our understanding of wakeful speech production as well. Box 1 summarizes some fun facts about sleep talking.

- Sleep talking happens at all ages and may occur during all parts of the night.
- Sleep talking is said to be more common in kids than in adults.
- The brain is not completely “switched off” during the night; otherwise sleep talking would not be possible.
- There are many songs about sleep talking and dreaming, for instance *Talking In Your Sleep* by The Romantics.
- Sleep talk is sometimes more creative than speech produced during the day!

BOX 1 - Some fun facts about sleep talking.

CONCLUSION AND OUTLOOK

In summary, there are many striking similarities between wakeful speech and sleep talk, but also some differences. Surprisingly, the study of sleep talking has not received much attention from scientists over the last 30 years. Many questions remain unanswered, and there is still a lot that needs to be discovered. Particularly, a good neurobiological account of the differences between sleep talk and wakeful speech in terms of the activation levels of brain networks involved in speech production is still lacking. Sleep talking may therefore be a great topic of study for a new generation of young minds.

GLOSSARY

Electroencephalography (EEG): A method that allows researchers and doctors to observe and

analyze brain activity by placing small sensors (“electrodes”) on a person’s scalp.

Frontal lobe: The part of the brain located at the front of the head, behind the forehead.

Hemisphere: The brain can be divided into a left part and a right part, which are separated by a large fissure. The two parts, which are connected, are called the left hemisphere and the right hemisphere.

Linguist: A person who studies language or different languages. Some linguists, for instance, describe languages that are only spoken by a small group of people. Others try to understand why a language changes over time. Unfortunately, not many linguists study sleep talking.

Neuroscientist: A person who studies the brain (and some other parts of the nervous system). Some neuroscientists, for instance, try to understand what happens in our brains when we are sleeping.

Temporal lobe: The part of the brain globally located above and behind the ears, in both *hemispheres*.

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Submitted: 24 February 2014; Accepted: 24 March 2014; Published online: 24 April 2014.

Citation: Peeters, D., and Dresler, M. (2014). Scientific significance of sleep talking. *Front. Young Minds.* 2:9. doi: 10.3389/frym.2014.00009

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REVIEWED BY:



Empress, 8 years old

I am crazy. I love chicken, gymnastics, soccer, and swimming. I like to talk with a British accent.



Maya, 10 years old

I love watching TV (Glee). I play basketball and soccer. Later, I like to be a professional videogame player. I like to cook. I am interested in sports medicine. I like to play drums and saxophone. I like to sing in front of a mirror.



Mika, 12 years old

I like cardiology. I like rock music, sci-fi movies, Game of Thrones, and to read adult books. I want to learn guitar.

AUTHORS



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Lives in The Netherlands. He studies how our brain allows us to use one or more languages and hand gestures to communicate. He likes running, cycling, sunshine, blueberries, and reading novels.



Martin Dresler

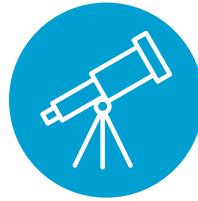
As a cognitive neuroscientist, I study the human brain and all the fun things we can do with it. I am particularly interested in how we learn and how we can improve our memory. In addition, I like to explore what happens in our brain when we sleep and dream.

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