

# Science AMA Series: I'm Seth Blackshaw, I study the brain and how it controls sleep and I'm reporting directly from the Society for Neuroscience Meeting in Washington DC. AMA!

HopkinsMedicineAMA<sup>1</sup>and r/ScienceAMAs<sup>1</sup>

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## Abstract

Hi Reddit, my name is Seth Blackshaw and I'm a professor of neuroscience at the Johns Hopkins University School of Medicine. My research focuses on identifying the network of genes that controls how different cell types in the hypothalamus are specified during embryonic development, and on using these findings to both identify how specific cell types regulate behavior and determine how they can be replaced in neurodegenerative disease. I became interested in this work because I am convinced that to understand how neural circuits work, we have to name and catalog their basic components – the thousands of different cell types present in the brain. If we can figure out how these cell types are made, we can then understand which behaviors they regulate and how they do so. We study development of the hypothalamus because it is a master regulatory center for many interesting and medically important behaviors – ranging from circadian timing to sleep to aggression. I recently published a paper on Nature describing newly identified brain cells in mice that play a major role in promoting sleep.. My team observed that a specialized type of neuron that had never been found in this area of the brain before appear to connect a part of the hypothalamus, called the zona incerta, to areas of the brain that control sleep and wakefulness. This discovery could lead to the development of new therapies to help people with sleep disorders, like insomnia and narcolepsy, which are caused by the dysfunction of similar sleep-regulating neurons. I look forward to answering your questions at 1pm ET

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Very simple question, but I'd like to hear your explanation: why do you think we need sleep? What function does it serve?

[wapkaplit](#)

That's not a very simple question, but we know that there are likely to have been three major stages in the evolution of sleep. The first is behavioral segregation of activity by time of day. All organisms that live on the surface of the Earth are either nocturnal or diurnal and specialized to that particular temporal niche. As a result, there are selective pressures to be inactive during the time of day that is opposite to the time of activity. This creates a period of forced inactivity. That period of inactivity wouldn't necessarily have to be sleep. This could be a sleep-like or inactive state. Sleep itself is the second stage of evolution. Synchronization to light-dark cycles occurs in all organisms, but sleep itself is exclusive to animals with a nervous system. It plays a restorative function. As neurons are active, synapses become more and more heavily potentiated. The nervous system needs to downscale across the board, during certain periods, as a homeostatic compensation for the active periods. Sleep pressure builds the longer an animal is active and thinking. During this period, toxic metabolites are removed from within neurons and energy stores are replaced. The third evolutionary stage is REM

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sleep, which is thought performs a cognitive function. REM sleep is sometimes called “dream” sleep, but this is not entirely true, because dreaming can occur anytime during sleep. REM sleep has been detected in reptiles, birds and mammals. Its function is not entirely clear, but seems to play a role in the consolidation of memories. It's not clear how dreams connects or packages those memories. During REM sleep, you can think of the brain as in a sensory deprivation tank; the hallucinations you'd experience closely resemble what could be experienced during dreaming.

Can a night shift worker get healthy sleep? If so, would it be a different amount?

[TheRealSquirrelGirl](#)

A night shift worker can, but the problem is that sleep controlled by two components - your circadian rhythm - your internal clock - & sleep pressure. The problem is that your sleeps needs to align with your work schedule. The longer you've been awake, the greater the pressure is to go to sleep. Because we are a diurnal species, that pressure is low in the morning and high at night. A shift worker has reversed that and their their biological clock is out of whack about 8 - 12 hours. During the night shift work, you are fighting the sleep pressure to not fall asleep and then at the end of their work time the circadian rhythm makes it harder to fall asleep. Their activity & their circadian rhythm is going to be out of sync until those aligned back again. During the alignment period, they will get less sleep and at a lower quality but eventually things will re-adjust. As in jet lag it takes roughly 1 hour per day to adjust. The problem with shift works is that the shifts change then you are back again on the adjustment phase.

Why does it become more difficult to have healthy sleep as one gets older? My wife who is in her 50s has no difficulty falling asleep, but often wakes up during the night and can't fall back asleep. The doctor said it is common at her age. Why does the brain do this to her? I, a man of the same age, don't have this problem. I feel bad because it is very frustrating for her. Good luck with your research.

[Bjarki56](#)

Thank you!

In general, we sleep less as we age and our sleep grows more fragmented. We still don't understand the reason for this, but we do know the core circadian clock, which resides in a tiny structure in the hypothalamus called the suprachiasmatic nucleus starts to malfunction as we age. The central clock keeps time less well and it communicates with the other parts of the brain that control functions such as sleep less efficiently. This may be the main reason why sleep becomes more fragmented.

What's the best way to alter one's sleeping pattern, i.e., switching from night shift to dayshift?

[thombudsman](#)

Several things can shift your body clock. First & foremost is light. You want to minimize light exposure when you are trying to sleep. If you are moving to a night shift in particular, buying shades or blackout curtains would help. Additionally, exposure to bright light when you wake up could be helpful. Food and exercise are also potent cues for resetting the core biological clock. Make sure to eat at the meal times in your reversed shift - no midnight snacking. And being active in the morning is also helpful for altering your clock. Also, to promoting sleep, sleeping aids can also help you fall asleep at the appropriate time & reduce sleep pressure during your shift. Likewise, mild stimulants like caffeine can help you stay awake.

Is there a good way to find out if you might have sleep apnea without going in for an expensive sleep study? I often feel unrested after a night of sleep and would like to find the cause.

[35mmFILM](#)

Feeling unrested is a common symptom of obstructive sleep apnea. First, I would say if you sleep with a partner, ask your partner if you snore, do you snore loudly & do you stop breathing when you are snoring. Are there periods when you gasp for breath? If so, you may have sleep apnea & I would recommend speaking with your doctor about a test. Being male, being overweight, having a thick neck & having sinus problems are all risk factors for apnea. If you have any of these risk factors & suffer from excessive daytime sleepiness, I'd suggest getting tested at a sleep lab. Treatment can vastly improve quality of life.

For more information about sleep apnea, go here:

[https://www.hopkinsmedicine.org/healthlibrary/conditions/adult/mens\\_health/sleep\\_apnea\\_85.P01301](https://www.hopkinsmedicine.org/healthlibrary/conditions/adult/mens_health/sleep_apnea_85.P01301)

What are some of the techniques and tools you use to identify the network of genes in the hypothalamus? Any computational ones?

[edwinks!](#)

Excellent question! We start by using unbiased techniques of gene expression analysis to comprehensively profile genes active in stages of hypothalamus development. We have used techniques such as microarray and RNA-seq analysis to identify genes that show increased expression at times when specific neuronal cell types are forming in the hypothalamus. Because of the extreme cellular complexity of the hypothalamus, we next use in situ hybridization to determine which specific cell types are expressing a gene of interest. With that information we then look at the genes we've identified and use genetic approaches to selectively disrupt that gene in the hypothalamus. We look to see the effect on the development of those cells and the effects on behavior in mature animals.

At present, we are now conducting single cell RNA-seq of developing hypothalamus. This requires fairly sophisticated computational approaches to identify and classify individual cell types and to identify changes of gene expression that drive development of individual cell types, particularly given the very large number of cells we have to analyze for this work.

Right now we are in the data gathering stage. The hypothalamus is extremely complex and we are nowhere near identifying all of the cell types. Once we have that information, we can begin using more computational methods to figure out what individual genes do.

My lab continues to work to optimize and troubleshoot these approaches using the retina, which actually emerges from the walls of the hypothalamus during development. It's an easier tissue to analyze because it has fewer cell types and a much more regular and well characterized structure.

Hey, thanks for taking the time to do this AMA!

Based on your research description ("...identifying the network of genes that controls how different cell types in the hypothalamus are specified during embryonic development"), it sounds like you also work on other processes and behaviors centered in the hypothalamus -- not just sleep. Could you share with us a couple of other discoveries or projects you've worked on that illustrate other biological "roles" for the hypothalamus and its circuitry? Thanks!

[kiri-kin-tha](#)

We work on the hypothalamus because it is a master regulator of a huge range of behaviors. First, we have identified genes that act as master regulators of the formation and function of the body's master clock, the suprachiasmatic nucleus. This affects not just sleep, but all physiological processes. We have also been investigating the function of a poorly characterized cell type known as tanycytes. Tanycytes are a form of radial glia found exclusively in the hypothalamus. They closely resemble neural progenitors in their shape & gene expression profiles & we found that they have a limited neurogenic potential. We have seen that a high fat diet can stimulate tanycytes to proliferate and give rise to cells that, in female mice only, regulate body weight. We are now studying the physiological function of tanycytes & tanycyte-derived neurons using genetic tools. As we study other genes that have interesting expression patterns in the hypothalamus, we inevitably get drawn into studying interesting and seemingly unrelated behaviors.

Hi Seth! I have a few questions.

- I am curious to know if there is an accurate method to determine how many hours of sleep will be necessary to feel completely reenergized in the morning? I currently sleep between 5-6 hours and am a morning person.
- Are there cells types that determine whether an individual likes to nap in the middle of the day? How can we regulate this behavior?

[dohiit](#)

The amount of sleep that any given person requires varies considerably, with an average around 7-8 hours. In otherwise healthy individuals it can vary from 5-11 hours. This has been seen in every animal we have studied and we have found that it is heavily influenced by genetics. If you are otherwise healthy, 5-6 hours should be fine - particularly for an older person.

Napping - a period of inactivity during the middle of the active phase (day for people) - is actually seen in most animals. Fruit flies & mice also like to nap. We don't know why, but we do know that the probability of napping increases with age as sleep becomes less consolidated.