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Why mice sleep longer than humans

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Most of us do it every night but we don't know why. If you miss too many nights, it might kill you.

We know why we eat, drink, breathe, and move around, but no one can explain why we need to sleep. What does seven or eight hours of snoozing really do for us? Van Savage at the Harvard Medical School and Geoffrey West of the Santa Fe Institute in New Mexico believe they have found a good answer.

One favorite explanation is that sleep is for resting the body. But as Steven Strogatz, a mathematician at Cornell University wisely points out, lying still for eight hours is no substitute for this strange state in which we spend decades of our lives "immobilized, unconscious, and vulnerable."

All mammals, from elephants to mice to humans, sleep, but in very different ways. Elephants get along on three to four hours, less than half of what humans require to stay healthy. Mice sleep about 14 hours a day. Whales keep one side of their brain awake while they sleep, allowing 1.5 hours of sleep per brain-side per day. The reason for sleep, then, must be tied to size.

It is also tied to metabolic rate, or the rate that energy is produced from food and enables animals to grow, fight, run, and reproduce. A woman is about 4,000 times the size of a mouse and has a metabolic rate that is 200 times larger. How exactly does this impact the need to sleep?

Surprisingly, no mathematical theory had ever been developed to explain how body size and metabolic rate are related to sleep. Such a theory would go a long way toward explaining the usefulness of sleep. So Savage and West constructed such a theory.

Their work yields predictions that correspond to different explanations of why we sleep. For example, if we sleep to rest our bodies, this would produce a different range of sizes than if sleep is needed only at the brain level.

Savage and West analyzed data on 96 different mammals, from the smallest to largest, shrews to whales. "We were able to distinguish between processes acting at brain level versus those on a whole-body level by using the fact that the brain does not increase in size as fast as the body. A horse is 10,000 times larger than a mouse but has a brain only about 1,000 times larger."

The fact that sleep times shorten rather than increase with body size, "is striking," Savage notes. "It is in distinct contrast to virtually all other biological rates and times, such as life span, gestation, and development of the young." For example, some whales reportedly live as long as 210 years, compared with humans who usually live 80-90 years, exceptionally long for our size. Mice have a life span of only about 2 years. Such a life span-to-size connection is likely tied to the function of sleep.

"Our data are consistent with the idea that sleep is primarily devoted to the critical activities of repair and reorganization in the brain, not the whole body, and that this reorganization probably includes learning and memory," says Savage. In the Jan. 16 issue of the *Proceedings of the National Academy of Sciences*, he and West report, "This leads to the conclusion that other organs and tissues do not require an analogous state because they can be repaired or reorganized during waking or resting periods."

The size of cells

Savage and West, along with Alex Herman at the University of California, San Francisco, and colleagues from other institutions next examined how the changes in the size of animals affect the size and metabolic rate of individual cells from which the animals are comprised. Their findings were published in the Feb. 26-March 2 online edition of the Proceedings of the National Academy of Sciences.

If you think about cells at all, you might suppose that a kidney cell from a mouse and a human would be identical. After all, they both have the same function, to rid the body of wastes. Humans are bigger and so have more wastes and more of these cells, but why should the individual cells be different?

The Savage team applied a key fact to answering this simple question. Just as the size of a brain does not increase as fast as the body it's in, an animal's metabolic rate does not increase as fast as body size. As noted before, a human, who is 4,000 times the size of an ordinary mouse, boasts a metabolic rate only 200 times greater.

"It follows that the metabolic rate per ounce for an average single cell must decrease as the body mass of the whole animal decreases," Savage explains. "There are two easy ways to do this, either the metabolic rate per cell changes while the cell size remains constant, or the cell size changes while metabolic rate stays constant. This dictates that a cell from a mouse and a human cannot be the same."

The Savage team set out to discover which of these two strategies apply to different cells, say a kidney and a brain cell. The researchers examined 18 different cell types from a variety of small and large mammals. As it turned out, most cells, including kidney, liver, lung, and red blood cells, keep their size constant while their metabolic rate rises or falls with size. However, a few cell types, especially brain and certain fat cells, increase their size as body size increases. In humans, our brain cells get slightly larger as we grow from infant to adult.

This situation raises the question of why some cells choose one strategy while others prefer a different "lifestyle." Savage and West speculate that, because brain cells are so rarely replaced compared with, say, kidney and blood cells, their numbers are set early in development, so they must grow as the body grows. Interestingly, this is also the reason that the brain needs a special system to maintain and repair itself. That special system is called "sleep."

"Most other cell types are frequently replaced during the life of an animal so they only have to work for a short time," Savage comments.

These things are fun to know and think about, but can they be applied in any way to help keep us healthy? "Definitely," Savage says. Take cancer, for example. Tumors grow out of control by developing their own system of blood vessels to feed themselves and maintain their metabolic rate. That drains resources from their host. Knowing how that system interfaces with the normal human cardiovascular system could aid in development of new ways to eliminate one system without harming the other. Herman is working with Savage and West to apply this idea to traditional cancer research.

Many cancer treatments, especially drugs, are tested on mice and rats before being tried on humans. To give us maximum benefit, it would be important to know more precisely how to scale up to humans the results in lab rats.

"Our findings also have potential applications to the spread of diseases where two species of different size carry the same virus," Savage notes. "The biological rates and processes of one species might be dynamically tied to the other species in ways that knowing about one would help us treat the other." Avian bird flu and malaria come to mind.

Savage says that he and others are exploring these possibilities.

Source: Harvard University