

The Night Shift

Sleep deprived pay the price for shift work

Trying to outsmart our circadian rhythms may have grim health results: obesity, cancer, mental illness and gastrointestinal problems.

By Shari Roan, Los Angeles Times Staff Writer; March 24, 2008

AT 6 a.m., the hospital's bright hallway lights flicker on, signaling the start of a new day. Doctors in crisp business clothes appear on their early-morning rounds, and the clang of breakfast carts will soon echo through the unit.

For registered nurse Liberty Bunag, however, it's finally time to go home and sleep. She began her shift 12 hours ago with an extra-large coffee and since has consumed a liter of caffeinated soda, more coffee and lots of rice, her personal energy food. Sometimes she and the other nurses on the orthopedic ward of White Memorial Medical Center in Los Angeles practice foreign languages to stay alert, squelching the yawns and drowsiness — the body's way of protesting this nocturnal activity.

Bunag's head throbs as she walks to her car. "When I get home," says the 26-year-old from Torrance, "my body is tired and my mind is exhausted."

In a 24/7 world, such fatigue passes for normal. Twenty percent of American workers are night-shift workers, and the number is growing by about 3% per year, according to the Bureau of Labor Statistics. While the rest of society sleeps, police officers, security guards, truck drivers, office cleaning crews, hotel desk clerks, nurses, pilots and many others keep patients alive, streets safe and packages moving. But at a price.

These workers — and people with more conventionally sleep-deprived lifestyles — are known to be at higher risk for accidents, sleep disorders and psychological stress due to daytime demands, such as family and other obligations, that interfere with sleeping. Now scientific evidence suggests their disrupted circadian rhythms may also cause a kind of biological revolt, raising their likelihood of obesity, cancer, reproductive health problems, mental illness and gastrointestinal disorders.

The evidence for an increased cancer risk is so compelling that, in December, the International Agency for Research on Cancer, a unit of the World Health Organization, declared that shift work is "probably carcinogenic to humans."

Researchers are beginning to understand why. Among the most significant — and startling — reasons: As much as 15% of human genes function on a schedule, with highly regulated, oscillating patterns of activity.

These clocklike genes are common features of most cells and can be found in every major organ in the body. They, in turn, affect the schedule of scores

of biological functions, from metabolism to cell division to cognitive processes.

"Less than 10 years ago, it was thought that sleep was for the brain and not for the rest of the body, so lack of sleep would make you tired, moody and more likely to have accidents," says sleep researcher Eve Van Cauter, a professor of medicine at the University of Chicago. "But sleep deprivation may be bad for the body too, representing a risk for a variety of abnormal conditions."

Evolution supports that theory. Life on Earth began with single-cell organisms that depended on sunlight for converting energy to food. "Life has been adapting to a light-dark cycle since the beginning of the planet," says Paolo Sassone-Corsi, chairman of the department of pharmacology at UC Irvine.

But modern humans wrongly think they can override their natural sleep patterns with impunity, says Dr. Charles Czeisler, director of the division of sleep medicine at Harvard Medical School. "It's a myth that we alone, among all animals, have the power to sleep when we want," he says.

Disrupted rhythms

Dennis Corrigan sometimes questions his decision to switch to a night shift 12 years ago.

By working nights, the UPS truck driver from West Covina, age 52, avoids the physical demands of the day shift, when lifting boxes is part of the job, plus the worst of L.A. traffic. The 10:45 p.m.-to-11 a.m. shift also allowed him to attend all of his son's high-school football games.

But Corrigan now sleeps only about six hours a day. He has put on weight and gets less exercise than before the switch and was diagnosed with diabetes five years ago.

"The rough part is, when I come home, I'm hungry," he says. "I eat a heavy meal before going off to bed. You're not supposed to do that. It's a worry."

His circadian rhythms may be to blame. Those rhythms determine when certain body processes take place. For example, melatonin, the hormone that aids sleep, is released at night; the hormone cortisol is low at night and pours out in the morning, jump-starting the body's daytime functions. But in night workers, melatonin continues to peak at night — even though they're awake — and cortisol levels continue to peak in the early morning hours, even when night-shift workers are eager to get some sleep.

Those disrupted circadian rhythms are why night-shift workers sleep less and with poorer quality, Van Cauter says: They try to sleep when their bodies want to be awake.

Chronic sleep deprivation may carry some of the same risks as disrupted circadian rhythms, she says. Today, Americans average about one hour less of sleep per night than they did 30 years ago.

Bunag feels the effect of night-shift work on her days off. If she tries to sleep at night, she often wakes around 3 a.m. and is alert until dawn, when she falls back to sleep, often for 10 hours. On work days, she sleeps about six hours during the day but still awakens tired.

“My problem is not while working but on my days off,” she says. “I feel unproductive because all I do is sleep all day, and I’m up the whole night when nothing much can get done.”

She finds herself less willing to socialize these days and worries that her irritability may border on depression. She also wonders about the long-term health consequences of her schedule. “I want to be able to sleep normally at night when the body does all of its detoxifying, cleansing, repairing and recharging. But I haven’t figured out what’s going to work for me.”

Her concerns are well-founded.

* Night-shift workers have a 40% to 50% increased risk of heart disease compared with day workers, various studies have found.

* People who get five hours of sleep, common among night-shift workers, are 50% more likely to be obese than normal sleepers, Columbia University researchers have found. Several dozen other studies have tied sleep loss to weight gain as well.

* Women night-shift workers have higher rates of miscarriage, pre-term birth and low birth-weight babies.

* Night-shift workers show increased rates of breast (by 50%) and colon (by 35%) cancer in numerous, independent studies. And animal studies have shown that exposure to dim light during the night-time can substantially increase tumor development.

“It’s been known for years that there is an increased risk of a variety of medical conditions in the population of shift workers,” says Dr. Diane Boivin, associate professor of psychiatry and director of the Centre for Study and Treatment of Circadian Rhythms at Douglas Mental Health University Institute in Montreal. “What is difficult to parcel out is the exact contribution of this circadian misalignment and sleep deprivation. We think it’s major, but it’s very difficult to be sure.”

Genes that keep time

Science is inching closer to understanding how a lack of sleep — or sleep at the wrong time — can wreak

biological havoc. In the last few years, researchers have made surprising discoveries about the body’s sophisticated time-keeping.

Scientists once assumed the body’s sole “clock” was nestled in a place in the brain called the suprachiasmatic nucleus, or SCN. Light — particularly sunlight — is the primary synchronizer for circadian rhythms. When we open our eyes each morning, light reaches photoreceptors in the retina and creates signals that travel to the SCN to jump-start the body’s hormones, neurotransmitters, temperature and metabolism for the new day.

But that’s not the body’s only timepiece. Circadian time-keeping genes can be found in organs all over the body. These peripheral clocks control the activity of many cellular processes and biological functions, and their presence may explain why sleep dysfunction seems to have such a broad effect on overall health. Light sets the circadian clocks in the SCN, but scientists still aren’t sure what compels the body’s peripheral clocks to work in unison. After all, the liver and the digestive tract don’t have direct access to sunlight.

“The SCN is like a musical conductor and the peripheral clocks are the instruments that need to play their music with peak activity at certain times of the day to get good harmony across the body,” Boivin says. “They must be in sync.”

The SCN somehow “talks” to these peripheral clocks by using hormones or other messengers, Van Cauter says.

For example, among its many functions, the nighttime release of hormone melatonin is thought to inhibit tumor growth. Melatonin production usually peaks in the middle of the night. But it stops being secreted when light reaches the eye in the morning — or when a light is switched on during the night.

This disruption could influence the genes involved in tumor development, Sassone-Corsi says, and provide a possible explanation for why cancer rates appear higher in shift workers.

How food can play a part

Food intake can also affect body clocks — and vice versa. The movement of glucose and nutrients through the bloodstream to organs affects appetite, digestion and metabolism. Travelers frequently encounter stomach and digestive difficulties when crossing time zones, for example, because food intake is in conflict with the time-keeping molecules in the body’s digestive system.

“When you’re a shift worker and displace your sleep, you also displace your feeding schedule,” Van Cauter says. The liver, pancreas and digestive system are not expecting food at the time that they’re getting it.

Sleep schedules that buck the body’s natural circadian rhythms can disrupt insulin production and

other hormones that are important to weight control, Van Cauter says. In a series of studies, she found that sleep-deprived adults produce more ghrelin, a hormone that promotes hunger, and less leptin, a hormone that suppresses appetite. Thus, the brains of tired people are sending out compelling messages to eat — especially foods that are starchy, sweet and high-carb.

Accordingly, people who sleep less may have more trouble keeping their blood sugar stable. In one of Van Cauter's studies, healthy young men were restricted to four hours of sleep per night for six consecutive nights and were found to have blood test results for insulin sensitivity so abnormal they almost matched those of diabetics.

Other research is exploring effects of sleep and shift work on neurotransmitters called orexins. These brain chemicals have unique, dual roles, making sure humans are alert when hungry to maximize food-seeking behavior.

After a big meal, fast-rising glucose levels in the body switch off orexin neurons, often making people feel sleepy — possibly an evolutionary response signaling humans to conserve energy after eating. "There is wiring in our brains that links feeding and being awake," Van Cauter says.

Thus, eating at midnight and sleeping at noon could lay the groundwork for the obesity, diabetes and heart disease seen more commonly in night workers. Moreover, as people age, they spend less time each night in phases of deep sleep. Van Cauter's research team is investigating whether this poorer-quality sleep may contribute to a variety of ailments in old age.

Preventing the damage

For people such as Bunag and Corrigan — and for society as a whole — night-shift work is a reality. "Our entire transportation infrastructure would break down if those trucks decided to use the roads during the day," Harvard's Czeisler says.

That's why, ultimately, scientists want to prevent the damage from shift work or insufficient sleep.

It's not easy, however, to tease apart the biological effect of disrupted circadian rhythms from other factors that may influence night-shift workers' health, such as poor diets, stress and lack of exercise. Many diseases, such as cancer and heart disease, are also influenced by risk factors that have nothing to do with occupation.

Moreover, individuals differ in how they cope with circadian rhythm disruption. As many as 10% adapt well, but 15% to 20% simply can't tolerate staying awake all night, according to Czeisler. The remainder cope, but with difficulty.

Sleep researchers have devised compensation tactics, such as the use of bright lights and melatonin supplements, to help night-shift workers remain alert on the job and sleep better after the shift. But the research on the body's molecular clocks may lead the way to better therapies, Sassone-Corsi says.

Identifying the molecular clocks that affect cell division, for example, may point the way to treatments to prevent cancer.

In a paper published in December in the journal *Nature*, Sassone-Corsi found that a single amino acid activates the genes that regulate circadian rhythms. This chemical switch could perhaps be manipulated by a medication of some sort to restore circadian rhythms that have gone awry.

"If we can explain how these molecules work, we can get targets" for potential therapies, he says. "We cannot beat the system, but we can work on it."

For now, however, researchers and sleep doctors alike implore people to show a little respect for slumber.

"People think of sleep as a waste of time," Sassone-Corsi says. "But it's essential. A correct sleep-wake cycle is as important to health as any other thing in our lives."

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