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# Chronobiology (part two)

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It was easy to theorize about how light and darkness affect plants because they need light, but it would take a particular kind of scientist to notice that other types of organisms, including mammals, also use light to alter their physiological function.

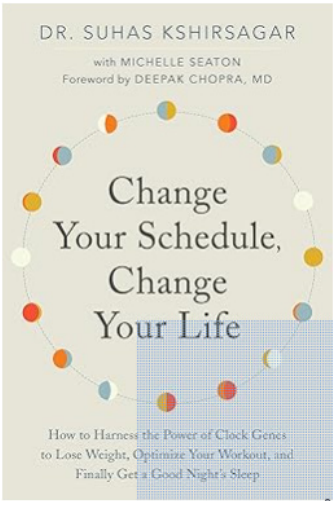
That scientist turned out to be a young Romanian doctor named Franz Halberg, who was completing a fellowship at Harvard in the late 1940s when he began to track the levels of circulating white blood cells in mice.

He continued his research at the University of Minnesota, where he noticed that the white blood cell count peaked during the day and fell at night. Different strains of mice had different levels of circulating white blood cells, but every type of mouse showed the same pattern of sharp rise during the day and a similar fall at night.

Soon, Halberg was tracking hourly fluctuations in blood pressure and heart rate in the mice, along with body temperature, and found that these physiological responses varied on a similar twenty-four-hour schedule. By 1959, he had coined the term "circadian rhythm" to account for these changes.

Over the ensuing decades, he theorized about and then proved similar variations in humans.

Halberg found that a host of physiological processes, including body temperature, hormone production, blood cell counts, blood pressure




and heart rate, glycogen levels in the liver, even cell division, all vary along predictable patterns, all of which seemed to him to be light-dependent.

But genetic research was still in its infancy, and few researchers wanted to believe that the body contained an internal clock that varied with time of day or with seasons of the year.

Halberg was certain that fluctuations within these patterns were possible markers for disease. He believed that monitoring blood pressure constantly gave a better prediction for heart attack and stroke than taking a single measure in a doctor's office. That's why he monitored his own blood pressure every thirty minutes each day for the last fifteen years of his life. Perhaps he was on to something. He lived to be ninety-four.

He further theorized that anticancer treatments would be most effective when the core temperature of tumors was highest. He believed that the body operated entirely on a circadian rhythm, and that nutritionists and medical doctors should consider these rhythms as part of any treatment plan. And although chronobiology centers sprang up in major research centers all over the world, it was difficult to prove the efficacy of these theories until the very end of the twentieth century. Halberg himself found it difficult to secure funding for his studies, and to get the subject of chronobiology taught in medical school.

It would be tempting to say that the rest of the medical community dismissed these theories. But the truth is that at the time it was expensive to constantly monitor blood pressure, blood counts, glucose uptake in the liver, and other physiological responses. Halberg's theories ranged far ahead of technology, and it would be up to geneticists to explore these ideas and figure out exactly how the cells in the body are able to coordinate with the SCN each day and night.

## Clock Genes

We now know that the cells in the body contain what are known as "clock genes." They have specific names, such as perl, per2, per3, which are active at night, or CLOCK and BMALl genes, which are active during the day.

They operate on a kind of loop. The activity of one of these clock genes inhibits the activity of the other. Your cells are primed to do different things based on the light and dark cycles of the day.

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And the protein pathways for each of these cells is active or inactive based on the time of day.

Every morning when you open your eyes and see daylight, your SCN is giving the signal to reset the internal clock and sends information to all of the systems of the body and all of the organs and tissues to say that it's daytime again. And this clock sets the automatic physiological changes that must occur on time for the next twenty-four hours in order for the body to function. In this way, the SCN is the brain's clock. Or perhaps we should say that it is the brain's master conductor, and all of your body's cells are trying to dance to its beat.

While the master clock in your brain is trying to set a total body rhythm, the cells in your body are reacting to your behavior—your sleep schedule, your mealtimes, and your activity to set their own clock rhythms. When the brain's clock and these cellular clocks—called "peripheral clocks"—are out of alignment, you can get distorted cell behaviors.

Remember those mice who gained weight when they were fed during their sleep cycle. Their bodies were operating outside the master circadian rhythm, taking in nutrients that the cells in their digestive tract couldn't process. And the reduced sleep schedule meant that on a cellular level, whole systems in their bodies stopped functioning the way they were supposed to. This causes disruptions not just in the digestive process, but in hormone production, immune response, and inflammatory response. As you can imagine, this puts an entirely new spin on the field of epigenetics and how our behavior alters and affects genetic expression over time.

As a field, chronobiology is still new, but clock genes seem to have an effect on aging and tumor suppression in addition to metabolism. Eating and sleeping at the wrong time disrupts the circadian rhythm and interferes with a healthy metabolism and a strong immune response. Though scientists are still working out many of the nuances and clinical treatment applications, what we know for certain is that you can use your daily schedule to reinforce the circadian rhythm and achieve better health. Even without the presence of light each morning, your body would try to function on that same twenty-four-hour schedule.

Starting in the 1970s, researchers did experiments with people who agreed to live in isolation without daily exposure to natural light. (Unlike de Mairan's plants, they agreed to go live in a cave.) A number of findings have emerged from these experiments over many decades.

First, the body's clock was adrift without the daily reset of natiural light and darkness. The primary means by which the body sets its circadian rhythm is through light. Second, the body can use social cues, such as timing of meals, sleep, and exercise, as a substitute when light signals are absent.

All of the body's attempts to synchronize its systems onto a single master circadian rhythm are called entrainment. The body relies on signals to help it reset the circadian rhythm and keep itself functioning optimally. While it prefers to use light and darkness as the primary signal, it can and does use other cues, including your behavior. Everything you do all day is either helping the master circadian clock to synchronize the body's functions, or it's getting in the way. Setting a daily schedule that reinforces your body's natural rhythm is the most powerful health habit you can adopt.

It's not just the human body that tries to set this daily rhythm. All of nature follows this same diurnal pattern. De Mairan's plants were opening their leaves in anticipation of light, even though the light never came to them. Their cells kept trying to keep the daily rhythm.

Many types of cells are tasked with doing one set of things in the daytime and another at night. This is true for mammals, for plants, and even for the smallest single-cell bacteria. In the past thirty years, genetic research and microbiology have transformed the study of these natural rhythms. Scientists have been working to discover clock genes inside of cells and how they work at the neurological and molecular level in all types of organisms.

Researchers are searching for the limit of the ways in which circadian rhythms rule biological systems in all living things, but they haven't found it yet. One researcher noted that it should be assumed that every system in the body works on a circadian rhythm until proven otherwise.