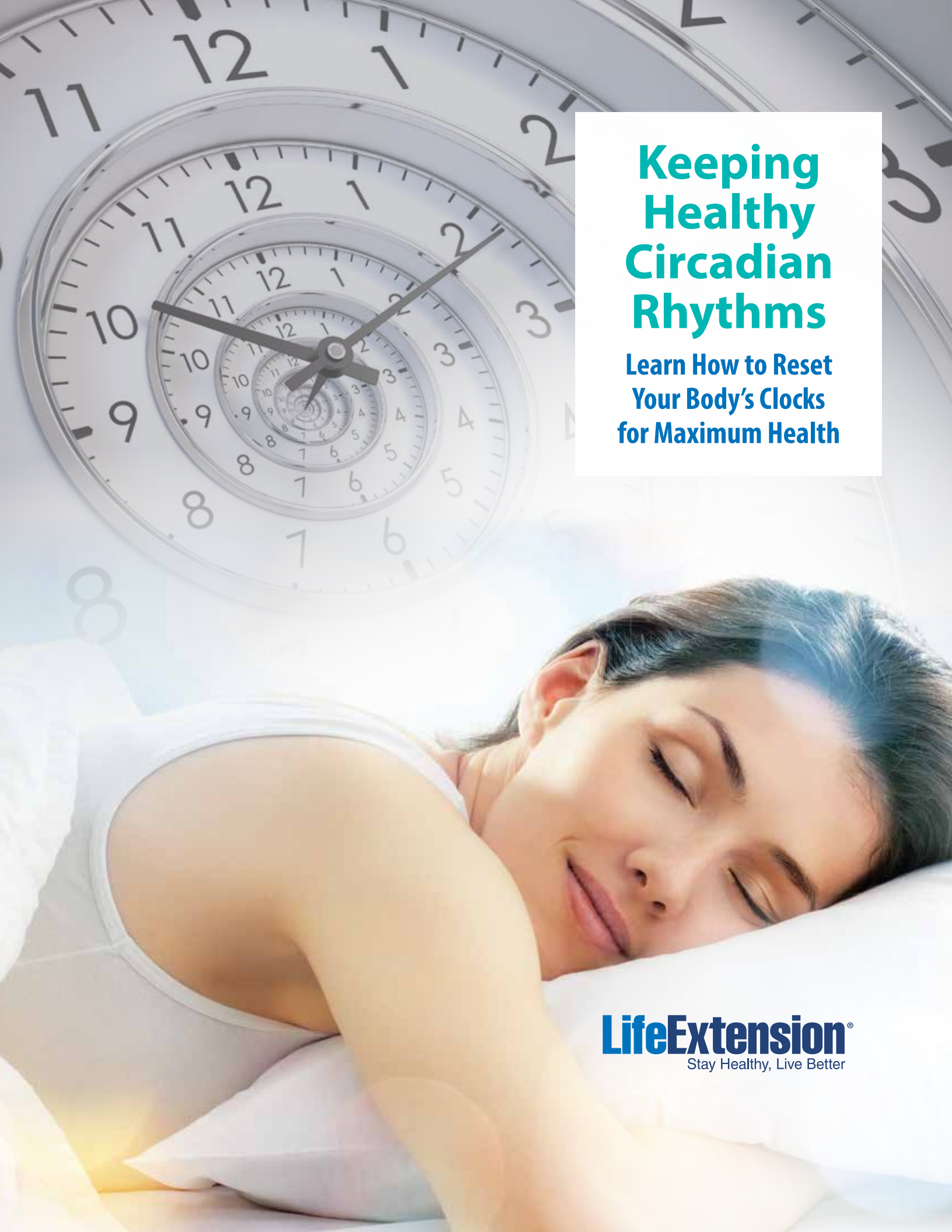

Keeping Healthy Circadian Rhythms

Learn How to Reset Your Body's Clocks for Maximum Health

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1 Circadian Rhythms & Your Health

Circadian rhythms aren't just about sleep cycles. In fact, circadian rhythms play a major role in your overall health — from blood pressure to metabolism. Find out what circadian rhythms are, how they're regulated by the clocks in your body — and how they impact your health.

2 Supporting Your Central Clock

Your central clock resides in your brain and regulates your sleep/wake cycles with some help from a hormone called melatonin. But unfortunately, our natural melatonin levels take a big dip as we age. Find out what you can do about it!

3 Supporting Your Peripheral Clocks

Peripheral clocks can be found throughout your body and — when functioning properly — they support good health in everything from your liver to your muscles. But what happens when they're not functioning properly? Discover a unique polyphenol that can keep your peripheral clocks on schedule — and promote your whole-body health!

1

Circadian Rhythms & Your Health

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Like many people, you've probably heard of circadian rhythms, and you may have an idea of what they're all about — something to do with sleep and sunlight, right? Well, that's a big part of it ... but there's actually much, much more.

In fact, circadian rhythms play an important role in a wide array of bodily functions — from heart rate to hormone regulation.

What Are Circadian Rhythms?

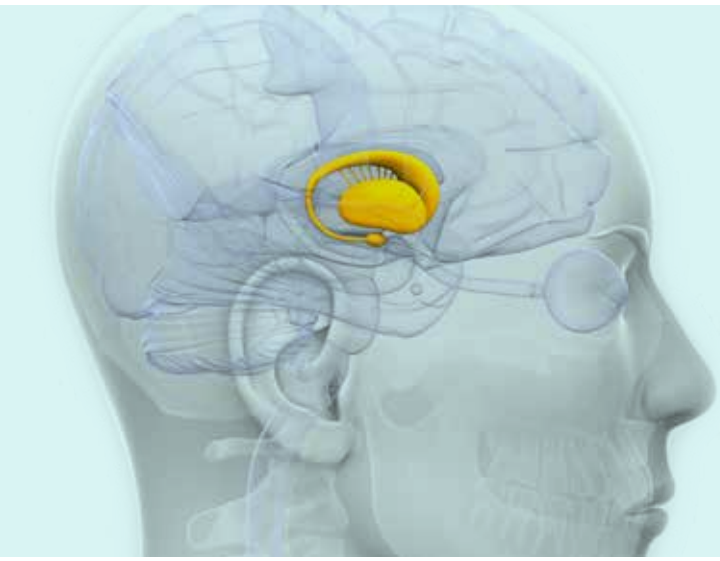
Circadian rhythms are 24-hour daily patterns of functions and behaviors, such as sleep, heart rate and blood pressure, body temperature, hormone levels, and metabolism.

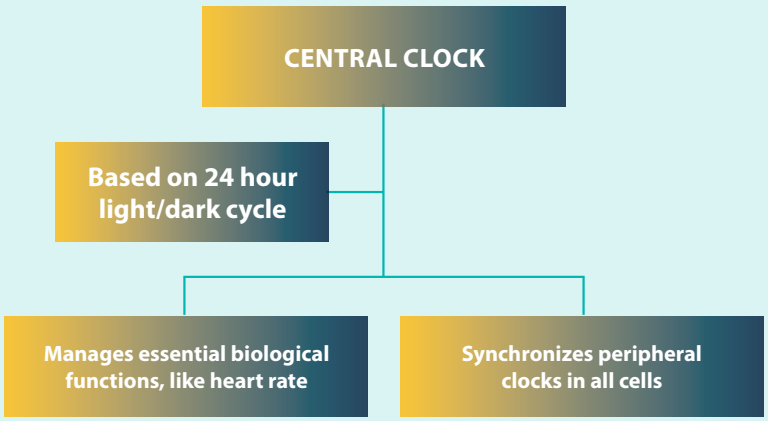
These rhythms are produced and regulated by an internal timekeeping system. There's one central clock in our brain and many peripheral clocks throughout our body.

About the Central Clock

Located in a part of the brain's hypothalamus — the part that controls essential basic functions such as temperature, heart rate, and blood pressure — the central clock regulates healthy sleep/wake cycles, which are vital to maintaining our overall health and wellness.

The natural day-light cycle sets the central clock's rhythm. In turn, the central clock synchronizes the rhythms of all the peripheral clocks.





About the Peripheral Clocks

Peripheral clocks are encoded in the DNA of almost every cell in your body — these are your circadian clock genes. Throughout a 24-hour cycle, the peripheral clocks establish a rhythmic ebb and flow that — when working properly — helps your body function for optimal health.

The peripheral clocks help regulate:

- Cell cycle and growth
- Cholesterol metabolism
- Immune response
- Fatty acid production
- Sugar metabolism

It's All About the Ebb and Flow

Feeling confused by the workings of circadian rhythms? Think of them like the ocean tides. The tidal forces of the Moon and Sun (the central clock) acting on the Earth (a peripheral clock) cause the cyclical rising and falling of Earth's ocean surface.

This ebb and flow of tides keeps the oceans healthy, having a tremendous impact on marine life.

There's a similar type of oscillation happening in the human body with circadian rhythms — except it's a 24-hour ebb and flow of function and behavior that supports our health.

Healthy vs. Unhealthy Clocks

Healthy clocks maintain the timing of essential processes, including sleep/wake cycles relative to light, liver function, blood pressure, and several behaviors such as learning, reward, and neurogenesis. When your clocks are healthy, all of your cells and organs work together to keep you and your body running smoothly.

But aging, your lifestyle and environment, and clock gene mutations can disrupt this process. The resulting **unhealthy clocks** can contribute to health issues such as cardiovascular disease, metabolic syndrome, obesity, diabetes, autoimmune disorders, cancer, and more.

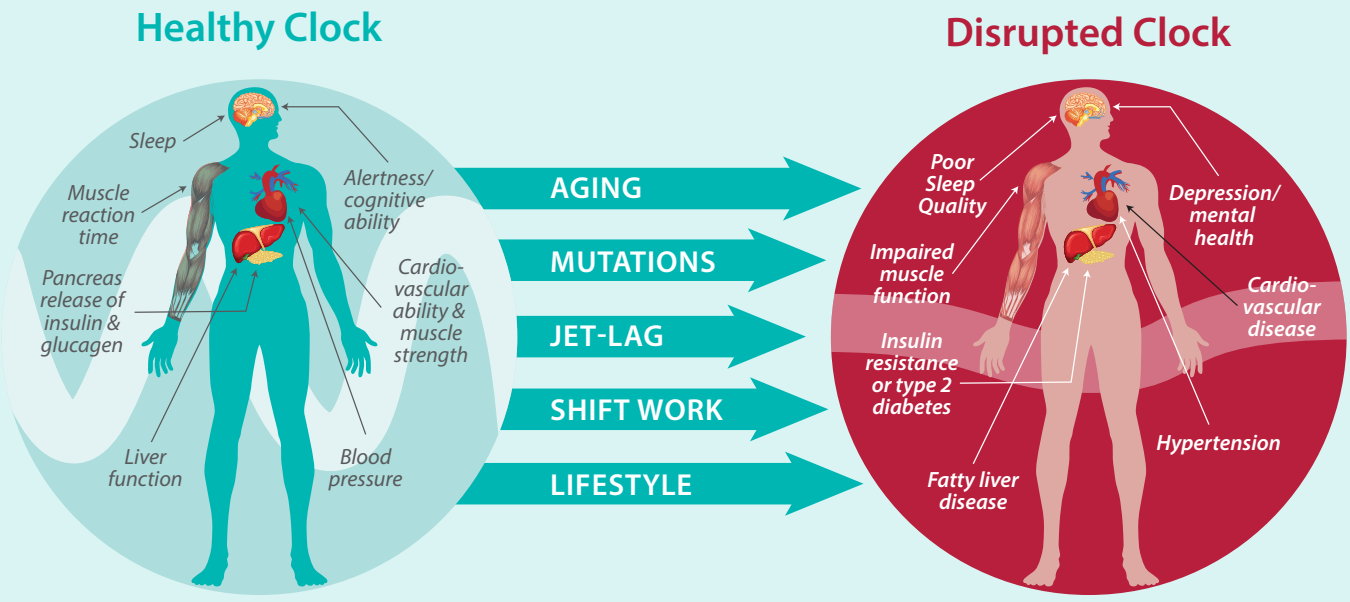
Fortunately, there's a way to reset your body's clocks — and restore your healthy circadian rhythms!

How Do You Know if YOUR Clocks Are Disrupted?

Be on the lookout for these signs — they could be telling you that it's time to reset your body's clocks.

- **You're sluggish in the late morning or early afternoon.** That's the period when you should be alert, so if you're having trouble getting going, it could be a sign of a disrupted clock.
- **You're a "night owl."** Humans are supposed to be preparing for sleep when the sun goes down, so if you have lots of energy at night, that could mean your clock is disrupted.
- **You have insomnia or any other sleep cycle problems.**
- **You do shift work.**

If you have any of these symptoms or you are obese and/or have diabetes or other metabolic issues, there's a good chance your body's clocks need to be reset.



2

Supporting the Central Clock

Supporting the Central Clock

Remember how the central clock is in the brain's hypothalamus — the part that manages essential life functions? This central clock resides in a tiny part of the hypothalamus called the supra-chiasmatic nucleus. That's a mouthful, so we can just call it SCN.

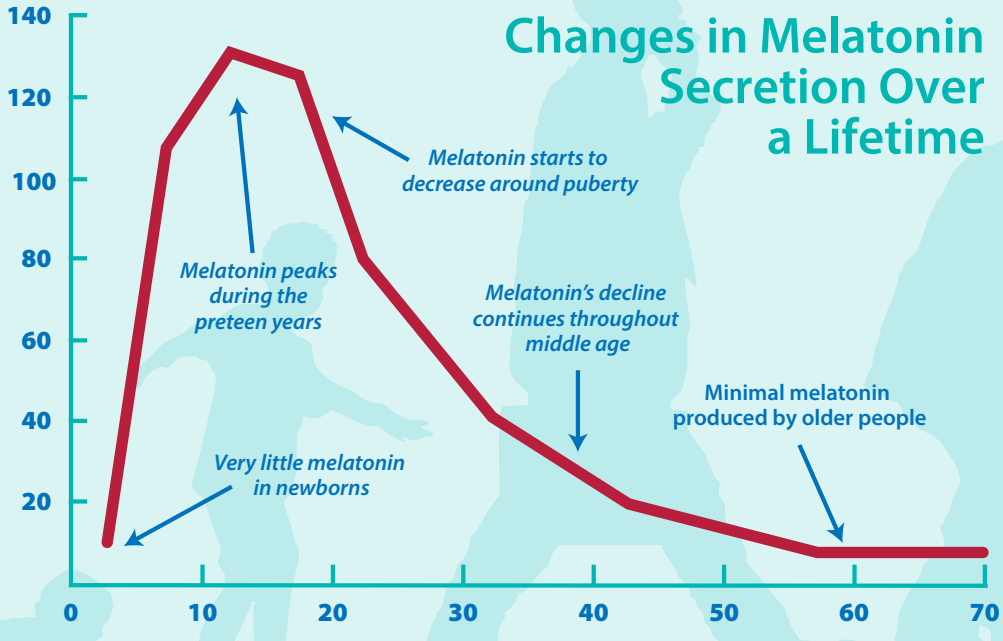
The SCN works with the hormone melatonin to help the central clock properly regulate sleep/wake cycles and coordinate with the peripheral clocks for whole-body health.

But here's the problem: our natural melatonin levels decrease significantly as we age. Take a look:

Reset the Central Clock with Melatonin

Since melatonin supports circadian sleep patterns— and since we know our melatonin levels decrease as we age — it makes sense to replace your natural supply of melatonin with a supplement.

Supplementing our melatonin levels helps regulate the sleep/wake cycle controlled by the central clock, which provides big benefits to our overall health and wellness.



Reference: https://scoliosisjournal.biomedcentral.com/articles/10.1186/1748-7161-2-6

3

Supporting the Peripheral Clocks

Supporting the Peripheral Clocks

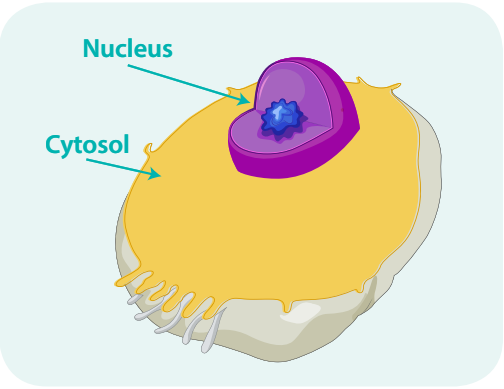
Peripheral clocks, and the circadian clock genes that maintain them, are found in cells all over your body — from liver cells to adrenal cells to muscle cells. And like all genes, circadian genes produce proteins.

The proteins produced by these circadian clock genes can be involved in anything from sugar metabolism to cell growth. Because these proteins are produced on a 24-hour cycle, the various functions they regulate also occur on a 24-hour clock.

How Does It Work?

A 24-hour cycle for a peripheral clock goes like this:

Step 1: In the nucleus of the cell (where your genes reside), the circadian clock genes turn on. These genes give instructions to the cellular machinery in the cell's cytosol (the fluid outside the nucleus but still inside the cell) that cause the production of their respective proteins



Step 2: These proteins build up throughout the day in the cell's cytosol. Once they reach a certain level, they cross over into the nucleus and turn off the circadian genes.

Step 3: Because the genes are turned off, the proteins are no longer being produced and soon reach a very low level. When that happens, the circadian genes turn back on and the cycle begins again!

This ebb and flow of genes turning on and off (like the tides, remember?) is the cellular circadian rhythm, helping to encourage healthy cellular functions.

Unfortunately, with age, bad sleep, and mutations to the circadian genes, this on-and-off process doesn't run as efficiently, which can then disrupt cellular function and health.

Reset the Peripheral Clocks with Nobiletin

Melatonin helps support the central clock, which aids the peripheral clocks as well. But we can also give the peripheral clocks some extra support — with a unique citrus extract called nobiletin.

Laboratory and animal studies have shown that nobiletin — a polyphenol antioxidant from citrus peel — acts on circadian genes to restore natural circadian rhythms. Basically, it can boost the expression of those genes to get that healthy ebb and flow going again.

In addition, nobiletin has been shown in lab and animal models to offer neuroprotection, cardiovascular protection, metabolic support, and inflammation-balancing support. While there is still more to learn, scientists believe that these benefits may well be in part the result of nobiletin's effects on circadian genes.

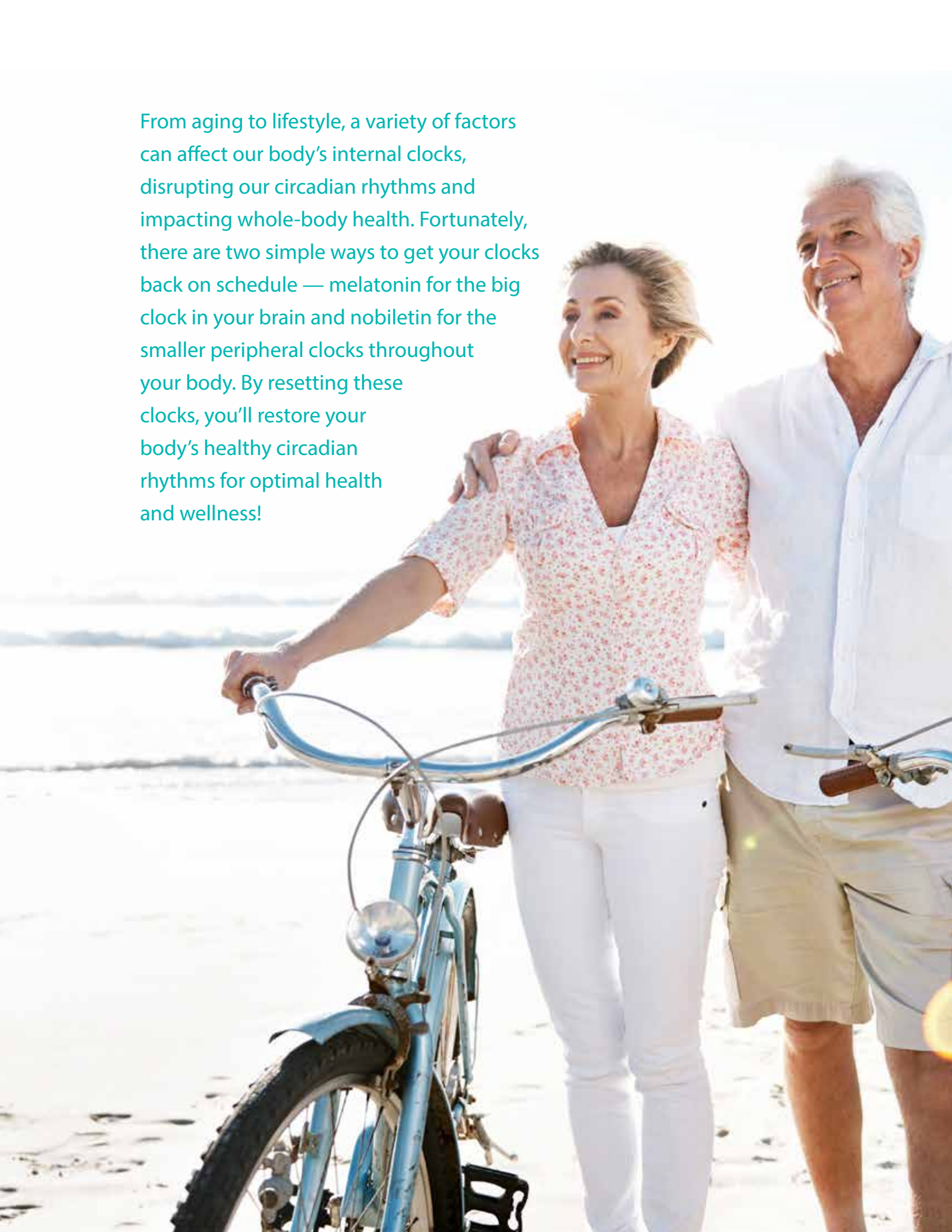
How Nobiletin Works

Nobiletin targets the RORs — retinoic acid–related orphan receptors. Normally these receptors, which are found throughout the body, provide the circadian clock with feedback from various processes in our bodies. Simply put, they are the link between body functions and the circadian clock genes.

But when the clocks are disrupted, the RORs lose their proper rhythms, creating whole body and metabolic havoc.

That's where nobiletin comes in — like a coach or drill sergeant who's ready to kick the lazy RORs into action! Nobiletin binds to the RORs and activates those receptors. Then the RORs get in gear and do their job — regulating the circadian rhythms and helping to control the body's circadian functions.

From aging to lifestyle, a variety of factors can affect our body's internal clocks, disrupting our circadian rhythms and impacting whole-body health. Fortunately, there are two simple ways to get your clocks back on schedule — melatonin for the big clock in your brain and nobiletin for the smaller peripheral clocks throughout your body. By resetting these clocks, you'll restore your body's healthy circadian rhythms for optimal health and wellness!



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