

APRIL 19, 2010

## Sleeping (or Not) by the Wrong Clock

By **MICHAEL TERMAN**

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All-Nighters is an exploration of insomnia, sleep and the nocturnal life.

### Tags:

[chronotherapy](#), [circadian rhythm](#), [insomnia](#), [melatonin](#)

Despite his best efforts, Cliff, 28, could not get to sleep until about 7 a.m. It had been this way since he was a teenager. He was a healthy and successful young scientist — except that he didn't arrive at the lab until 5 p.m., just as his co-workers were preparing to leave. Although he got his work done by pulling all-nighters, he became isolated from the group. Sleeping pills didn't work. Nighttime alcohol bouts got him to sleep sooner, but only by two to three hours — a bummer on many levels. Significantly, Cliff was not depressed.

George, a 34 year-old paralegal, had a much more common experience. He could rarely sleep until 1:30 a.m. Inured to sleeping pills, he would get into bed at midnight, hoping for the best. He had to be awake at 7:30 in order to make it in by 9, but it was a losing battle. Almost always late, he remained foggy until afternoon, and suffered headaches. Unlike Cliff, George was mildly depressed.

Cliff and George, whose names have been changed here to protect their privacy, are two of hundreds of patients we've treated at the Center for Light Treatment and Biological Rhythms at Columbia University Medical Center (where I serve as clinic director), and in research trials supported by the National Institute of Mental Health and the Sleep Research Society Foundation at the New York State Psychiatric Institute (where I have been a principal investigator).

Both Cliff and George were treated using chronotherapeutics — methods designed to reset the internal circadian clock.<sup>[1]</sup>, <sup>[2]</sup> George was dealing with sleep onset insomnia, a problem for millions of people. We inferred clinically that his circadian clock signal for sleeping was delayed relative to local time. People sleep best when the internal clock is in sync with the workday rest/activity cycle. When there is a mismatch, the likely results are insomnia, depressed mood and daytime fatigue.

An unbalanced circadian rhythm can be returned to equilibrium through the application of light to a sleeper's retina near the end of a person's "internal night." *Internal night?*

Yes — it may be night outside, but if your circadian clock is not prepared for sleep, internal night may not start until late and last well into morning. Biologically, it coincides with the secretion of melatonin by the brain’s pineal gland. It is difficult to know where your internal night lies if you artificially force sleep earlier, for example with sleeping pills. You can estimate internal night with a quick chronotype questionnaire [3] that helps determine when light exposure will be most effective for syncing your circadian rhythm with external reality.

George began therapy at 8 a.m every day with 30 minutes of 10,000 lux bright light. [4] This had no effect. But when we switched the timing to 7:30, he immediately started getting to sleep an hour earlier, by 12:30 a.m. However, he began waking up far too early, before 6 a.m. This indicated an overdose of light. When we reduced light exposure to 15 minutes, still at 7:30 a.m., he began falling asleep at midnight and waking up just before alarm (a few minutes before the scheduled light exposure). Within a week of starting treatment, his depression lifted, he was more alert in the morning and his headaches vanished. Lesson learned: just as with drugs, light therapy needs to be individually dosed, which may require a clinician’s guidance.

Cliff, who usually slept between 7 a.m. and 3 p.m., was following his internal clock, though he was out of sync with the outer world. His sleep problem cleared up in two weeks using a combination of three chronotherapeutic methods. First, he began light therapy upon waking in mid-afternoon. As his internal clock began to respond, he was able to wake up earlier for the lights in 30-minute steps.

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Second, we administered a minute dose (0.2 milligrams) of sustained-release melatonin about five hours before bedtime, mimicking the action of the pineal gland, before it begins its nightly cycle. [4] This dosage is in sharp contrast to over-the-counter melatonin, which usually comes in megadoses (3 to 5 milligrams) that deliver far more hormone than the pineal gland ever produces. The mini-dose does not act like a sleeping pill, so you spend the evening awake and alert. Rather, it communicates with the circadian clock in the same way as morning light exposure, shifting internal night earlier.

Finally, after taking melatonin, Cliff wore specially filtered wraparound glasses [1] that prevent inappropriate evening light from acting against morning light exposure. He soon found it easy to sleep from 11:30 p.m. to 7:30 a.m. Then he was off to the gym and into the lab. He was incredulous: “I thought my circadian clock was permanently damaged!”

Cliff’s case is instructive because even with greatly delayed sleep onset, he was not depressed; his sleep patterns obeyed his internal clock. George, by contrast, struggled to sleep earlier on a biologically inappropriate schedule — often a major factor underlying

depression. With light and melatonin therapies, we can shift the internal night into congruence with local time and the workday schedule, with dual antidepressant and sleep-enhancing results.

Depression, of course, can become overwhelming, far more severe than it was for George. And sleep itself actively feeds severe depression — a vicious cycle that needs to be broken. A therapeutic full night awake under observation in a hospital setting instantly relieves the depression in about 60 percent of patients. This is one of the major, surprising findings of biological psychiatry. The problem is, after the next day's recovery sleep the depression is likely to return. So the benefit is only ephemeral.

To counter the relapse, we begin daily light therapy at the end of the wake therapy night, enabling the circadian clock to readjust, with the result of sustained remission. [1] The benefit is enhanced with a very early bedtime the night after wake therapy, and early rising after recovery sleep. In patients with bipolar disorder, the effect is further magnified by the use of lithium carbonate, the mood-stabilizing drug.[5] A manic reaction is very rare, but it can be quickly dampened by staying in a darkened room for 14 hours. Such dark therapy can be just as effective as anti-manic (anti-psychotic) medication.[6]

In American psychiatry, chronotherapeutics is a new kid on the block, viewed by some as a counter-intuitive departure from conventional medication. By contrast, in Europe, where it is already well established, it is seen as compatible with medication and a means for expediting improvement with fewer residual symptoms. Residual symptoms are harbingers of relapse. To protect our patients, we should be pulling out all the stops.

Footnotes:

[1]. Anna Wirz-Justice, Francesco Benedetti, Michael Terman, "Chronotherapeutics for Affective Disorders: A Clinician's Manual for Light and Wake Therapy," Basel, S. Karger, 2009.

[2] Olivia Judson, "[Enter the Chronotherapists](#)," New York Times, December 22, 2009.

[3] Michael Terman, Thomas White, Joy Jacobs, "[Automated morningness-eveningness questionnaire](#)."

[4] Michael Terman, Jiuan Su Terman, "Light therapy, in Principles and Practice of Sleep Medicine," 5th ed., Meir Kryger, Thomas Roth and William Dement (Eds.), Philadelphia, Elsevier, 1682-1695, 2010.

[5] Cristina Colombo, Adelio Lucca, Francesco Benedetti, Barbara Barbini, Euridice Campori, Enrico Smeraldi, "Total sleep deprivation combined with lithium and light therapy in the treatment of bipolar depression: replication of main effects and

interaction,” *Psychiatry Research* 95(1), 43-53, 2000.

[6] Barbara Barbini, Francesco Benedetti, Cristina Colombo, Danilo Datoli, Alessandro Bernasconi, Mara Ciagala-Fulgosi, Marcello Florita, Enrico Smeraldi, “Dark therapy for mania: a pilot study,” *Bipolar Disorders* 7(1), 98-101, 2005.

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