

Fitful nightly sleep linked to chronic inflammation, hardened arteries

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Disrupted nightly sleep and clogged arteries tend to sneak up on us as we age. And while both disorders may seem unrelated, a new study from the University of California, Berkeley, helps explain why they are, in fact,

pathologically intertwined.

UC Berkeley sleep scientists have begun to reveal what it is about fragmented nightly sleep that leads to the fatty arterial plaque buildup known as atherosclerosis that can result in fatal heart disease.

"We've discovered that fragmented sleep is associated with a unique pathway—chronic circulating inflammation throughout the blood stream—which, in turn, is linked to higher amounts of plaques in coronary arteries," said study senior author Matthew Walker, a UC Berkeley professor of psychology and neuroscience.

The findings, published June 4 in the journal *PLOS Biology*, adds poor sleep as a key risk factor for cardiovascular disease, which ranks as the top killer of Americans, with some 12,000 deaths each week—although COVID-19, which has killed, on average, 1,000 a day during the pandemic in the U.S., comes close.

"To the best of our knowledge, these data are the first to associate sleep fragmentation, inflammation and atherosclerosis in humans," said study lead author Raphael Vallat, a postdoctoral researcher in Walker's Center for Human Sleep Science at UC Berkeley.

Established risk factors for cardiovascular disease in humans include poor diet, lack of exercise, obesity, high blood pressure and smoking.

Using statistical modeling, the researchers analyzed the diagnostic data of more than 1,600 middle-aged and older adults using a national dataset known as the Multi-Ethnic Study of Atherosclerosis.

To isolate the effect of sleep quality on heart health, the study controlled for age, ethnicity, gender, body mass index, sleep disorders, blood pressure and high-risk behaviors such as smoking.

The researchers then tracked the results of the study participants, analyzing their blood tests, their calcium scores that can gauge plaque buildup, as well as several different measures of sleep, including wristwatch-assessed sleep across a week and a night in a sleep laboratory that measured electrical brainwave signals.

The final outcome clearly linked disrupted sleep patterns to higher concentrations of circulating inflammatory factors and, specifically, of white blood cells known as monocytes and neutrophils, which are key players in atherosclerosis.

"In revealing this link with chronic inflammation, the findings suggest a missing middleman that is brokering the bad deal between fragmented sleep and the hardening of blood vessels," Walker said.

"Indeed, these associational results in humans mirror recent data in which experimentally manipulated sleep disruption in mice led to higher levels of circulating inflammation that caused atherosclerotic lesions in the rodents," added Vallat.

The findings linking poor sleep to atherosclerosis via chronic inflammation have major public health implications, researchers said.

For example, atherosclerosis often begins in early adulthood.

"Unfortunately, this process goes largely unnoticed until the plaque buildup, in middle or old age, suddenly blocks arterial blood flow to the heart, lungs, brain and/or other organs, hence its moniker, 'silent killer,'" said Vallat.

"The insidious nature of the disease requires that we pay attention to our sleep hygiene, even starting in early to midlife," said study co-lead author Vyoma Shah, a doctoral student in Walker's lab.

To more accurately gauge one's sleep quality, the researchers recommend the use of clinical grade sleep trackers, because the study found that people's subjective assessments of their sleep were not reliable.

"If you track your sleep patterns using objective measures, the same way you track your weight, blood pressure or cholesterol, you can make modifications to your sleep habits, which could make a tangible difference to later life health outcomes," said Shah.

With chronic inflammation shaping up to be a bridge connecting poor sleep to cardiovascular disease, it's worth exploring its role in a plethora of other diseases where inflammation is known to be a possible factor, the researchers said.

"This link between fragmented sleep and chronic inflammation may not be limited to heart disease, but could include mental health and neurological disorders, such as major depression and Alzheimer's disease," Walker said. "These are new avenues we must now explore."

Tips to improve sleep quality

- Maintain a regular sleep routine, going to bed and waking up at the same time each day.
- As part of a nightly wind-down routine, avoid viewing computer, smartphone and TV screens in the last hour before bedtime, and keep phones and other digital devices out of the bedroom.
- Engage in some form of physical exercise during the day.
- Get exposure to natural daylight, especially in the first half of the day.
- Avoid stimulants, like caffeine, and sedatives, like alcohol, later in the day.
- If you can't sleep, get out of bed and do a relaxing activity away

from the bedroom, such as reading in dim light. Only return to bed when you're sleepy.

- Get screened for sleep apnea if you are known to be a heavy snorer and/or feel excessively tired during the day.
- Consult your doctor if you are experiencing insomnia, and inquire about cognitive behavioral therapy for insomnia (CBTI).

More information: Vallat R, Shah VD, Redline S, Attia P, Walker MP (2020) Broken sleep predicts hardened blood vessels. *PLoS Biol* 18(6): e3000726. doi.org/10.1371/journal.pbio.3000726

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