Painkillers might not work if you are sleep deprived, study suggests

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New research uncovers unexpected links between sleep deprivation and pain sensitivity. The findings may have significant implications for pain management therapies.

A recent study from the National Institutes of Health (NIH) estimates that more than 25 million adults in the United States live with chronic pain, and almost 40 million adults have experienced severe pain in the past 3 months.

Any pain that lasts for longer than 12 weeks is considered to be chronic. Chronic pain can be a consequence of injury, an underlying illness, or it may have no known cause.

Many people resort to complementary medical practices such as yoga or meditation to ease the pain. New research, however, examines the link between sleep deprivation, pain sensitivity, and common painkillers, and finds surprising connections. In the future, these findings could help patients with chronic pain to better manage their discomfort.

The study was carried out by researchers at Boston Children's Hospital and Beth Israel Deaconess Medical Center (BIDMC), both in Boston, MA, and their findings were published in the journal *Nature Medicine.*

Studying the link between sleep deprivation and pain in mice

The team - co-led by brain physiologist Alban Latremoliere, Ph.D., and sleep physiologist Chloe Alexandre, Ph.D. - investigated the impact of acute and chronic sleep deprivation, as well as the resulting sleepiness, on sensitivity to painful and non-painful stimuli.

They also examined the effect of common painkillers such as ibuprofen and morphine, alongside the effect of wakefulness-promoting drugs such as caffeine and modafinil, on pain sensitivity.

At the beginning of the study, the team monitored the sleep cycles and sensory sensitivity of between six and 12 mice using small headsets that took electroencephalography and electromyography measurements. This provided the researchers with baseline data.

The researchers then found a way to deprive the mice of sleep in a manner that was not stressful: by entertaining them. To replicate what happens when humans stay up too late, they distracted the mice with toys and fun activities when they were supposed to be asleep.

They were careful to prevent the mice from sleeping without overstimulating them. The mice were kept awake for either 12 hours straight, or for 6 hours during 5 successive days. Throughout these periods of wakefulness, the researchers monitored sleepiness, stress levels, and tested for pain sensitivity.

Sensitivity to painful stimuli was measured by applying controlled amounts of heat, cold, or pressure to the mice. Additionally, the rodents were also exposed to capsaicin - the active compound in hot chili peppers.

The researchers measured how long it took the mice to move away from the painful stimuli, or how long before they started licking away the pain caused by the hot chili compound.

Sensitivity to non-painful stimuli was tested by startling the mice with a sudden, loud noise and observing their response, which was usually to jump.

Pain killers do not work, but caffeine does

The study revealed a strong connection between sleep deprivation and pain sensitivity.

> "We found that 5 consecutive days of moderate sleep deprivation can significantly exacerbate pain sensitivity over time in otherwise healthy mice. The response was specific to pain, and was not due to a state of general hyperexcitability to any stimuli."
>
> Chloe Alexandre, Ph.D.

Probably the most surprising finding was that common painkillers seemed to have no efficacy in alleviating pain induced by sleep deprivation.

Neither ibuprofen nor morphine could prevent or stop the effects of the hypersensitivity induced by sleep loss.

By contrast, wakefulness-promoting drugs successfully stopped the pain hypersensitivity caused by acute and chronic sleep deprivation.

However, modafinil and caffeine did not have pain-relieving properties in the mice that had slept normally.

The findings suggest that patients with chronic pain who use common painkillers may have to increase their dose if they are also sleep deprived, which may introduce side effects. Fatigue and sleep disorder often accompany chronic pain.

The researchers say that their findings may pave the way for a new type of painkiller.

> "This represents a new kind of analgesic that had not been considered before, one that depends on the biological state of the animal. Such drugs could help disrupt the chronic pain cycle, in which pain disrupts sleep, which then promotes pain, which further disrupts sleep."
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> Clifford Woolf, study co-author

The researchers also recommend that patients with chronic pain complement their painkillers with sleep-inducing medications at night and drugs that keep them alert during the day, in an attempt to break the pain cycle.

Dr. Kiran Maski, sleep disorders specialist at BIDMC, also weighs in on the findings, saying, "Many patients with chronic pain suffer from poor sleep and daytime fatigue, and some pain medications themselves can contribute to these co-morbidities."

She adds, "This study suggests a novel approach to pain management that would be relatively easy to implement in clinical care. Clinical research is needed to understand what sleep duration is required and to test the efficacy of wake-promoting medications in chronic pain patients."

Learn how brain differences between men and women affect response to pain relief.