

Inflammation can lead to circadian sleep disorders

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Inflammation, which is the root cause of autoimmune disorders including arthritis, Type 1 diabetes, irritable bowel syndrome and Crohn's disease, has unexpected effects on body clock function and can

lead to sleep and shiftwork-type disorders, a new Northwestern Medicine study in mice found.

The study was published in the journal *Genes & Development*.

The study used a new technology—a genetic switch—to turn inflammation on and off in genetically modified mouse models. When researchers deactivated inflammation, the mouse was unable to tell what time it was and was unable to keep an intact rest-activity cycle.

In addition to this new technology, the study was novel because, for the first time, scientists saw a link between what causes inflammation and what controls the body's clock.

In [inflammatory diseases](#), the body experiences an excess of a genetic factor known as NF-kappa beta (NFkB), the study found. NFkB is a catalyst for a set of chain reactions, or pathway, that leads to the pain and tissue destruction patients feel in inflammatory diseases. That same chain-reaction catalyst also controls the body's clock.

"NFkB alters the core processor through which we tell time, and now we know that it is also critical in linking inflammation to rest-activity patterns," said senior author Dr. Joseph Bass, the Charles F. Kettering Professor of Medicine and director of the Center for Diabetes and Metabolism at Northwestern University Feinberg School of Medicine.

When people have sore muscles and take an ibuprofen to reduce the inflammation, they are essentially trying to turn down the activation of inflammation, which is similar to what the authors did in this study, Bass said.

The findings also have implications for diet and provide a detailed roadmap to understanding the fundamental mechanisms by which

inflammation—including the inflammation that occurs when someone chronically consumes a high-fat diet—and likely other instigators lead to circadian disorders.

The scientists sought to understand how a high-fat diet might affect the perception of time at the tissue level, which is what led to their study of inflammation, said first author Hee-Kyung Hong, research assistant professor of endocrinology at Feinberg.

One of the reasons Western diet contributes to diabetes, cardiovascular disease and even certain cancers is thought to be the inappropriate trigger of inflammation, so a unifying idea is that impaired time-keeping may be one of the links between diet and disease.

"We don't know the reasons, but this interaction between the inflammation and clocks is not only relevant to understanding how [inflammation](#) affects the brain and sleep-wake cycle but also how immune or fat cells work," Hong said.

The study is titled, "Requirement for NF- κ B in Maintenance of Molecular and Behavioral Circadian Rhythms in Mice."

More information: Hee-Kyung Hong et al, Requirement for NF- κ B in maintenance of molecular and behavioral circadian rhythms in mice, *Genes & Development* (2018). [DOI: 10.1101/gad.319228.118](https://doi.org/10.1101/gad.319228.118)

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