Eating at Night and Sleeping by Day Swiftly Alters Key Blood Proteins

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Summary: Researchers report proteins associated with immunity and metabolism can become disrupted following just one simulated night shift.

Source: University of Colorado Boulder.

Staying awake all night and sleeping all day for just a few days can disrupt levels and time of day patterns of more than 100 proteins in the blood, including those that influence blood sugar, energy metabolism, and immune function, according to new University of Colorado Boulder research published in the journal *PNAS* this week.

"This tells us that when we experience things like jet lag or a couple of nights of shift work, we very rapidly alter our normal physiology in a way that if sustained can be detrimental to our health," said senior author Kenneth Wright, director of the Sleep and Chronobiology Laboratory and Professor in the Department of Integrative Physiology.

The study is the first to examine how protein levels in human blood, also known as the plasma proteome, vary over a 24-hour period and how altered sleep and meal timing affects them.

It also pinpointed 30 distinct proteins that, regardless of sleep and meal timing, vary depending upon what internal circadian time it is.

The findings could open the door for developing new treatments for night shift workers, who make up about 20 percent of the global workforce and are at higher risk for diabetes and cancer. It could also enable doctors to precisely time administration of drugs, vaccines and diagnostic tests around the circadian clock.

"If we know the proteins that the clock regulates, we can adjust timing of treatments to be in line with those proteins," said lead author Christopher Depner, a postdoctoral researcher in the Department of Integrative Physiology.

The researchers recruited six healthy male subjects in their 20s to spend six days at CU's clinical translational research center, where their meals, sleep, activity and light exposure were tightly controlled.

On days one and two, the men stuck to a normal schedule. Then they were gradually transitioned to a simulated night-shift work pattern, in which they had eight hour sleep opportunities during the day and stayed up all night, eating then.

Researchers drew blood every four hours and used technology recently developed by Boulder-based SomaLogic, Inc to assess levels and time-of-day-patterns of 1,129 proteins. They found 129 proteins whose patterns were thrown off by the simulated night shift.

"By the second day of the misalignment we were already starting to see proteins that normally peak during the day peaking at night and vice versa," Depner said.

One of those proteins was glucagon, which prompts the liver to push more sugar into the bloodstream. When subjects stayed awake at night, levels not only surged at night instead of day but also peaked at higher levels. Long-term, this pattern could help explain why night-shift workers tend to have higher diabetes rates, Depner said.

The simulated night shift schedule also decreased levels of fibroblast growth factor 19, which has been shown in animal models to boost calorie-burning or energy expenditure. This fell in line with the finding that subjects burned 10 percent fewer calories per minute when their schedule was misaligned.

Thirty proteins showed a clear 24-hour-cycle, with the majority peaking between 2 p.m. and 9 p.m. The takeaway: When it comes to diagnostic blood tests – which are relied upon more often in the age of precision medicine – "timing matters," said Wright.

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The study is the first to examine how protein levels in human blood, also known as the plasma proteome, vary over a 24-hour period and how altered sleep and meal timing affects them. NeuroscienceNews.com image is in the public domain.

Previous studies have looked at time-of-day expression patterns of protein-coding genes in specific organs. By studying the actual proteins in the blood, researchers can study a broader array and get a better picture of what's happening in real time, Depner said.

He and Wright note that they kept all the study subjects in dim light conditions, so that light-exposure (which can also strongly affectthe circadian system) didn't influence results. Even without the glow of electronics at night, changes in protein patterns were rapid and widespread.

"This shows that the problem is not just light at night," Wright said. "When people eat at the wrong time or are awake at the wrong time that can have consequences too."

ABOUT THIS NEUROSCIENCE RESEARCH ARTICLE

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Abstract

Mistimed feeding and sleep alters 24 hour time-of-day patterns of the human plasma proteome

Proteomics holds great promise for understanding human physiology, developing health biomarkers, and precision medicine. However, how much the plasma proteome varies with time of day and is regulated by the master circadian suprachiasmatic nucleus brain clock, assessed here by the melatonin rhythm, is largely unknown. Here, we assessed 24-h time-of-day patterns of human plasma proteins in six healthy men during daytime food intake and nighttime sleep in phase with the endogenous circadian clock (i.e., circadian alignment) versus daytime sleep and nighttime food intake out of phase with the endogenous circadian clock (i.e., circadian misalignment induced by simulated nightshift work). We identified 24-h time-of-day patterns in 573 of 1,129 proteins analyzed, with 30 proteins showing strong regulation by the circadian cycle. Relative to circadian alignment, the average abundance and/or 24-h time-of-day patterns of 127 proteins were altered during circadian misalignment. Altered proteins were associated with biological pathways involved in immune function, metabolism, and cancer. Of the 30 circadian-regulated proteins, the majority peaked between 1400 hours and 2100 hours, and these 30 proteins were associated with basic pathways involved in extracellular matrix organization, tyrosine kinase signaling, and signaling by receptor tyrosine-protein kinase erbB-2. Furthermore, circadian misalignment altered multiple proteins known to regulate glucose homeostasis and/or energy metabolism, with implications for altered metabolic physiology. Our findings demonstrate the circadian clock, the behavioral wake–sleep/food intake–fasting cycle, and interactions between these processes regulate 24-h time-of-day patterns of human plasma proteins and help identify mechanisms of circadian misalignment that may contribute to metabolic dysregulation.

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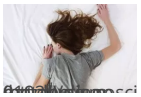

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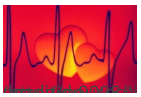

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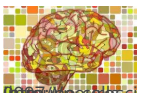

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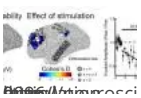

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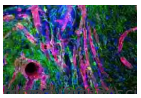

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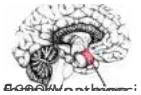

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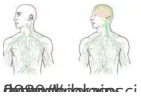

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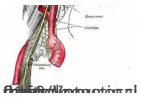

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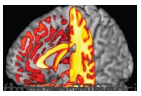

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