Biological 'Clock' Influences Damage Done by Oxidative Stress

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(PhysOrg.com) -- Swing shift workers and frequent fliers beware – scientists have identified yet another biological issue that relates to the "circadian clock" found in almost every species from insects to humans, and discovered that the time of day also affects the ability to resist oxidative stress.

In a new study just published by researchers from Oregon State University, it was found that fruit flies had their greatest ability to manage oxidative stress in the early morning, shortly before they had to deal with the challenges of the day – and the least natural defense in late afternoon or evening, a time when DNA damage reached its peak.

When the gene that controls this process was completely removed by genetic manipulation, the fly's ability to deal with oxidative stress essentially disappeared.

Oxidative stress can occur during the normal metabolism of oxygen, when levels of "reactive oxygen species" become too high, normal defense mechanisms break down and cell damage results. This is an issue in several significant health concerns, ranging from heart disease to Alzheimer's disease, premature aging and cancer. It now appears that animals, through the genetics that control their circadian rhythms, have natural ebb and flow in handling oxidative stress based on time of day.

The studies examined the role of the gene "period" in fruit flies, which is already known to influence reproduction, sperm release, sleep cycles,

drug sensitivities, learning ability, and other biological functions. Oxidative stress management can now be added to the list – the study concluded that "the circadian clock gene 'period' is essential for maintaining a robust anti-oxidative defense."

This is the first report of this type of rhythmic susceptibility to oxidative stress, the study said. The research was led by Jaga Giebultowicz, an OSU associate professor of zoology.

"In fruit flies, the ability to deal with oxidative stress was very significant," said Natraj Krishnan, a research associate at OSU and co-author on the new publication, in Biochemical and Biophysical Research Communications.

"That doesn't automatically tell us what the effects would be in humans, but our ability to deal with oxidative stress is very important to our health," Krishnan said. "This could be a concern to people who routinely have disrupted sleep cycles, such as swing shift workers, people who work at night, travelers crossing time zones."

Almost all organisms on Earth have evolved with a reaction to the rhythmic changes in light from day to night, Krishnan said, and organize their activities in a time-related pattern called "circadian rhythm." But research in recent years is just beginning to understand how powerful these rhythms are, with physiological, biochemical and behavioral functions linked to them. The "clock" genes that control them have also been found to influence other critical life functions – sleeping, feeding, reproduction, and now disease prevention. As a reflection of its evolutionary persistence and importance, the "period" gene is found in many animal species and expressed in almost every cell in the human body.

"There has been what some call a clockwork explosion of interest in this

field," Krishnan said. "These genes seem to influence or control so many different metabolic functions, and disruption of those functions may have serious health implications."

Much of the research is being done with the fruit fly because its genome has been completely sequenced and many of its genes perform the same function as in higher animals, including humans.

The practical use of information in this area is still being developed, Krishnan said. The efficacy of some cancer treatment drugs has already been found to be largely dependent on the time of delivery. Mental acuity is not the same throughout the day, and it may be that individuals learn best at specific periods. And in humans it has been found that the risk of death from various pathologies varies with time of day.

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