'Biological clock' could be a key to better health, longer life

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This fruit fly is used by researchers at Oregon State University for studies of the genes that control the "biological clock" in this and many other animal species, including humans. Photo courtesy of Oregon State University.

If you aren't getting a good, consistent and regular night's sleep, a new study suggests it could reduce your ability to handle oxidative stress, cause impacts to your health, increase motor and neurological deterioration, speed aging and ultimately cut short your life.

That is, if your "biological clock" genes work the same way as those of a fruit fly. And they probably do.

In research just published in the journal *Aging*, scientists from Oregon State University outline for the first time how a key gene that helps control circadian rhythms can improve the health of aging fruit flies if it is intact, but can result in significant health impacts, up to and including

earlier death, if it is absent.

Of particular interest, the research found, was that young fruit flies without this gene were able to handle some stress, but middle-aged and older flies were not.

"We're beginning to identify some of the underlying mechanisms that may help explain why organisms age," said Natraj Krishnan, a research associate in the OSU Department of Zoology. "This study suggests that young individuals may be able to handle certain stresses, but the same insults at an older age cause genetic damage and appear to lead to health problems and earlier death. And it's linked to biological clocks."

It's not completely clear how closely the effects of genetic damage in fruit flies correlate to humans and other animals, Krishnan said, but "the genes themselves, their molecular mechanisms and function is essentially the same, conserved through many millions of years of evolution." The "period" gene in fruit flies, for instance, is also found and expressed in almost every cell in the human body.

This research examined that gene, which is one of four primary genes that help control the biological clock in many animals - the rhythms that are related to the cycle of day and night, and can be disrupted by anything from inadequate sleep to jet lag or working the swing shift. The study used some normal fruit flies and other mutant flies in which the "period" gene was absent.

The work was done under the leadership of Jadwiga Giebultowicz, an OSU professor of zoology, in collaboration with Dr. Doris Kretzschmar from the Oregon Health and Sciences University. The research was supported by the National Institutes of Health and the Oregon Partnership for Alzheimer's Research.

In control studies, the mutant flies with no functional "period" gene lived just about as long as normal flies, unless they were stressed. In experiments, researchers caused a mild metabolic stress - an elevated level of reactive oxygen species for 24 hours - to the flies at various times, which corresponded to their youth, middle age and old age. There was no significant change in the young flies. But in middle-age and older flies, significant damage began to occur.

Mutant flies lost some of their motor ability to climb, and morphologic examinations of their brains showed higher levels of neuronal degeneration, similar to neurodegenerative diseases such as Alzheimer's disease in humans. When exposed to a single stressful event in "middle age," the mutant flies had a 12 percent shorter lifespan than normal flies exposed to the same stress. And when exposed to a single stress in old age, their lifespan was 20 percent shorter.

The study concluded that expression of the "period" gene naturally declines with age. If the same is true for humans, that could help explain why people may lose some of their ability to handle oxidative and other stresses at a time of their life when they need it most.

The scientists theorized that the "period" gene is regulating pathways involved in removal of oxidative damage, and those without this function experienced the symptoms of aging more quickly. This could ultimately have impacts on everything from neurological damage to heart disease and cancer.

"What's worth noting, of course, is that every animal species, unless they are in a protected laboratory, experiences stressful events," Krishnan said. "That's part of a normal life. The metabolic challenge we presented to these fruit flies was only a moderate stress. But even so, it appeared to later cause motor and neuronal degeneration and an earlier death in the mutant flies, due to faster buildup of cellular damage."

Further research will explore ways in which biological clocks might be "re-vitalized."

"Understanding these mechanisms will help to determine in the future whether strong circadian clocks add water to the fountain of youth," the researchers wrote in their conclusion.

Provided by Oregon State University