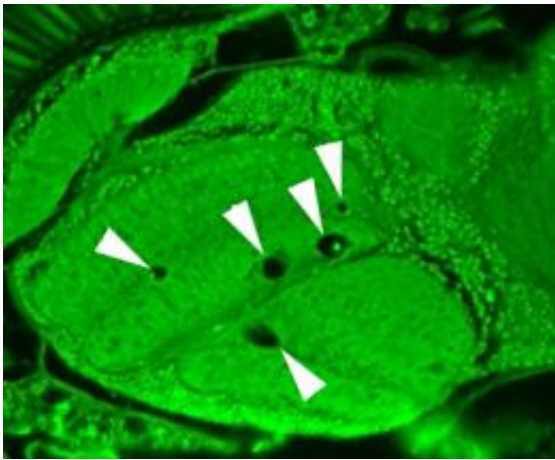


Disruption of biological clocks causes neurodegeneration, early death

January 10 2012



An increased number of "vacuoles," or holes in the brain, indicate neuronal damage and appear in fruit flies with disrupted biological clocks. (Photo courtesy of Oregon State University)

New research at Oregon State University provides evidence for the first time that disruption of circadian rhythms – the biological "clocks" found in many animals – can clearly cause accelerated neurodegeneration, loss of motor function and premature death.

The study was published in *Neurobiology of Disease* and done by researchers at OSU and Oregon Health and Science University. Prior to this, it wasn't clear which came first - whether the disruption of biological clock mechanisms was the cause or the result of

neurodegeneration.

"In these experiments, we showed through both environmental and genetic approaches that disrupting the biological clock accelerated these health problems," said Kuntol Rakshit, an OSU graduate fellow.

"There's a great deal of interest right now in studies on circadian rhythms, as we learn more about the range of problems that can result when they are disrupted," Rakshit said. "Ultimately we hope that this research will be taken from the laboratory to the bedside."

These studies were done with fruit flies, but the OSU scientists said previous research has indicated there are close parallels between them and humans. Some of the genes regulating circadian rhythms in flies are so important that they have been preserved through millions of years of separate evolution and still do the same thing in humans.

The biological clock, in humans and many other animals, is a complex genetic mechanism tuned to the 24-hour day and regular cycles of light, dark and sleep. It influences a wide range of biological processes, from fertility to hormone production, feeding patterns, DNA repair, sleep, stress reactions, even the effectiveness of medications. In humans, researchers have found strong correlations between disrupted clock mechanisms, aging, and neurologic diseases such as Alzheimer's and Huntington's disease.

The fruit flies used in this research carried two mutations, one that disrupts [circadian rhythms](#) and another that causes flies to develop brain pathologies during aging. These double mutants had a 32-50 percent shorter lifespan, lost much of their motor function, and developed significant "vacuoles" or holes in their brains far sooner than flies with a functional clock.

The decline and loss of clock function may be just the beginning of a damaging, circular process, said Jadwiga Giebultowicz, an OSU professor of zoology, member of the OSU Center for Healthy Aging Research and project leader.

"When the biological clock begins to fail, rhythms that regulate cell function and health get disrupted, and we now know that this predisposes the brain to neurodegeneration," Giebultowicz said. "But that [neurodegeneration](#), in turn, may cause more damage to the clock function.

"A healthy biological clock helps protect against this damage," she said. "When the clock fails, the damage processes speed up."

Aging is closely associated with this process, Giebultowicz said, but it's not clear exactly how. Molecular clock oscillations decline during aging. Finding ways to restore them might form a possible therapy for [biological clock](#) damage and help to prevent disease, and work in that area will be part of future research.

More information:

ir.library.oregonstate.edu/xmlui/handle/1957/26511

Provided by Oregon State University

Citation: Disruption of biological clocks causes neurodegeneration, early death (2012, January 10) retrieved 10 May 2024 from <https://medicalxpress.com/news/2012-01-disruption-biological-clocks-neurodegeneration-early.html>

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