Mice suffer from a decrease in biological fitness if their internal clock is mixed up

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For more than a year scientists investigated the development of six groups of mice in an outdoor enclosure. Credit: © MPI f. Ornithology

Mice with deviant internal rhythms due to a genetic mutation have fewer offspring and shorter life spans than normal conspecifics whose rhythms follow the 24-hr cycle of a day more accurately. This discovery was made by a team of scientists led by researchers from the Max Planck Institute for Ornithology and Princeton University. Internal clocks that generate daily rhythms in living beings are among the most important achievements on earth. They are essential for coordinating processes of life with the environment. The study on mice shows that a deviation of internal rhythms from the 24-hr rotation of the earth has a direct influence on biological fitness.

Almost all living things possess internal clocks that govern periods of sleep and waking, and ensure that these processes are in synchrony with night and day. This circadian clock evolved to allow the anticipation of regular daily events. Sunlight aligns the internal clock with the 24-hour-rhythm of the rotation of the earth. A fundamental, unanswered question so far has been: is the functioning of the internal clock important for how long an organism lives and how well it is able to reproduce in its natural environment?

Mutations in certain genes can disrupt the internal clock so that it runs out of sync with the day-night cycle. In mice, a mutation called tau is known to alter daily rhythms: mice carrying this mutation run through their day about two hours faster than normal mice. Scientists from the Max Planck Institute for Ornithology in Seewiesen and Radolfzell together with colleagues from the University of Groningen, the University of Manchester and Princeton University studied the biological fitness of such mice with deviant circadian rhythms in a large outdoor enclosure for over a year, where they were exposed to natural predators. At the beginning of the study the researchers divided 238 mice into six groups. For each group they housed an identical mix of mice without the mutation together with mice carrying either one or two copies of the mutation in their genes. Each mouse was equipped with a transponder, so

that the scientists could monitor their activity rhythms at feeders. Mice with one or two copies of the mutation showed aberrant daily rhythms.

Mice without the mutation were observed to live longer and to produce more offspring than mice with the mutation that showed abnormal rhythms. As a consequence, after more than one year the prevalence of the mutation in the population dropped from an initial 50 percent in the starting population to only about 20 percent in the last cohort that was studied. This finding led the researchers to conclude that strong selection pressures must exist against the tau mutation in a natural environment. "Our findings highlight the fundamental importance of circadian clocks for the biological fitness of living beings. This has never been shown that clearly", summarizes senior author Michaela Hau.

More information: Kamiel Spoelstra, Martin Wikelski, Serge Daan, Andrew Loudon, Michaela Hau, Natural selection against a circadian clock gene mutation in mice. *PNAS*; 28 December, 2015. www.pnas.org/cgi/doi/10.1073/pnas.1516442113

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