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Study: Sleeping sickness not just a sleeping disorder

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An international study from the Instituto de Medicina Molecular shows one of Africa's most lethal diseases is actually a circadian rhythm disorder caused by the acceleration of biological clocks controlling a range of vital functions besides sleep. By understanding which clock genes are affected by the parasitic disease, scientists hope the research will eventually prove useful in developing therapeutic alternatives to the toxic treatments that are occasionally fatal to patients.

"This is not specifically a sleeping disorder (feel free to adjust, delete this quote as desired)," said Dr. Luisa Figueiredo, Group Leader at Instituto de Medicina Molecular.

Sleeping sickness—known as human African trypanosomiasis—is transmitted through the bite of the tsetse fly and threatens tens of millions of people in sub-Saharan African countries. After entering the body, the parasite causes such symptoms as inverted sleeping cycles, fever, muscle weakness, and itching. It eventually invades the central nervous system and, depending on its type, can kill its host in anywhere from a few months to several years.

The mouse study published in *Nature Communications* shows sleeping sickness symptoms can occur soon after infection, even before parasites accumulate in large numbers in the brain. Scientists found that the biological clocks in infected mice ran faster after parasites entered the blood stream, resulting in inverted sleeping cycles as well as hormone and body temperature abnormalities similarly seen in patients with

sleeping sickness.

However, not all parasitic diseases appear to be circadian rhythm disorders: The biological clocks of mice infected with malaria were unaltered. "What we still need to find out is exactly what is causing the clocks to change during sleeping sickness. Is it a secretion from the parasite, or a molecule produced by the host in response to the infection? Knowing the source will help us have a better understanding of the disease and potentially block such effects." said Dr. Figueiredo, who was recently awared a grant from the European Research Council.

The study is the second recent collaborative effort between Dr. Figueiredo and Dr. Joseph Takahashi at the UT Southwestern, Dallas, USA. It builds upon research they published last year that showed for the first time that parasites have biological clocks. The study further showed that this circadian cycle renders the sleeping sickness parasite—known as Trypanosoma brucei—more vulnerable to medications during the afternoon.

Both findings could eventually be beneficial for patients whose bodies can't handle side effects of the arsenic-based treatments used to eradicate the parasite. In addition to knowing which genes to target when developing new therapies, doctors hope the findings will allow them to reduce the duration and dosage of current treatments by knowing the optimal time to administer them.

Meanwhile, control efforts have significantly reduced the number of cases over the last decade. However, an unknown number of people still die annually from sleeping sickness as scientists continue seeking vaccines and alternative treatments.

More information: Filipa Rijo-Ferreira et al, Sleeping sickness is a circadian disorder, *Nature Communications* (2017). DOI:

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