Therapeutic agent reduces age-related sleep problems in fruit flies

1 April 2014

The fruit fly *Drosophila melanogaster* has a life expectancy of approx. 8 weeks and belongs to the model organisms studied by scientists at the Max Planck Institute for Biology of Ageing in their quest to understand aging in living beings. Credit: MPI f. Biology of Ageing/ W. Weiss

Elderly flies do not sleep well – they frequently wake up during the night and wander around restlessly. The same is true of humans. For researchers at the Max Planck Institute for Biology of Ageing in Cologne, the sleeplessness experienced by the fruit fly *Drosophila* is therefore a model case for human sleeping behaviour. The scientists have now discovered molecules in the flies' cells that affect how the animals sleep in old age: if insulin/IGF signalling is active, the quality of the animals' sleep is reduced and they wake up more often. Using a therapeutic agent, researchers managed to improve the flies' sleep again. The scientists suspect that the causes of sleep problems experienced by older flies and humans are similar. It is also possible that sleep problems encountered by humans may not necessarily be an inevitable side effect of ageing and may even be reversible.

Flies and humans sleep in much the same way. Just like us, flies sleep during the night and are active during the day. And the quality of sleep deteriorates as both species age: the individuals nap more frequently during the day and sleep for shorter periods at night.

Gerontologists are very familiar with the insulin/IGF (insulin-like growth factor) signalling pathway. It is actually a metabolic pathway that controls the cell's response to nutritional deficiency and also affects life expectancy. Fruit flies therefore live longer if the signalling pathway is less active. The signalling pathway also plays a role in ageing humans.

Researchers at the Cologne-based Max Planck Institute have now discovered that fruit flies sleep better at night and are more active during the day if insulin/IGF signalling is inhibited. "Daytime activity and night-time sleep are thereby controlled by two different components: during the day, the neurotransmitter octopamine and the adipokinetic hormone AKH increase activity in flies. At night, on the other hand, the neurotransmitter dopamine and the kinase TOR reduce the sleep periods," explains Luke Tain from the Max Planck Institute for Biology of Ageing.

Rapamycin is a substance that inhibits TOR activity, inhibiting the molecule. "We administered rapamycin to older flies and observed that they once again slept for longer periods. As a result, we were able to reverse the deterioration in sleep quality as a consequence of ageing," says Tain.

The cells of such different organisms as roundworms, flies and humans use the insulin/IGF signalling pathway. Its components and function are similar in various species of living organisms. The researchers now want to study whether the signal molecules in higher animals, such as mice, have the same effect. In this way, they hope to discover treatments that will improve sleep quality in old age.

More information: Athanasios Metaxakis, Luke S. Tain, Sebastian Grönke, Oliver Hendrich, Yvonne Hinze, Ulrike Birras & Linda Partridge , Lowered Insulin Signalling Ameliorates Age-Related Sleep Fragmentation in Drosophila , *PLoS Biology*, 2 April 2014. www.plosbiology.org/article/in … journal.pbio.1001824

Provided by Max Planck Society