

## Mediobasal hypothalamus transmits the time of feeding to locomotor activity

Rina Nunokawa<sup>1</sup>, Hikari Yoshitane<sup>1</sup>, Shigenobu Shibata<sup>2</sup>, Yoshitaka Fukada<sup>1</sup>

<sup>1</sup>Department of Biophysics and Biochemistry, The University of Tokyo, Japan, <sup>2</sup>Physiology and Pharmacology, Waseda University, Japan.

In mammals, temporal restriction of feeding induces a food anticipatory activity (FAA), which is postulated to be controlled by a food-entrainable oscillator (FEO). FEO does not depend on circadian clock systems in the suprachiasmatic nucleus (SCN), because FAA is not perturbed by SCN ablation or by deficiency in some of the essential clock genes. However, the localization and molecular mechanism of FEO have still remained elusive. Here we found that the locomotor activity of mice was upregulated a few hours before feeding time under scheduled restricted feeding, in which meal was provided only in light phase (L-RF). The FAA was also induced by dark-phase restricted feeding (D-RF). In this condition, expression profiles of PER2 protein in a peripheral tissue showed anti-phase rhythms between L-RF and D-RF when the bioluminescence from the liver slice of PER2::Luc knock-in mice was continuously monitored. Intriguingly, expression rhythms of clock genes in the mediobasal hypothalamus (MBH), a candidate region for FEO, responded to feeding schedules rather than to light-dark cycles, while SCN was synchronized only light-dark cycles. Together, these data suggest that MBH plays a significant role as FEO and transmits the time of feeding to locomotor activity.