University of Fribourg / Faculty of Science and Medicine / Department of Chemistry

Clocks, Feeding and Mood

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Organisms have evolved in such a way that certain aspects of behaviour and biochemical signalling are limited to specific times of the day, which increases their efficiency and reduces energy demands. To achieve time-dependent signalling in an organism, a molecular clock needed to evolve to regulate downstream rhythmic processes. In mammals, this results in a clear separation of activity and rest periods, specific times of feeding when food availability is potentially higher and risk of becoming food is lower, and different levels of alertness during one single day. It also makes sense that fine tuning of mammals may favour time-controlled regulation of molecules involved in more complex behaviours, such as mood-related behaviours.
The effects of the molecular clock on adaptation to feeding time and mood-related behaviours have been previously reported, but many unknowns remain.
A prerequisite of adaptation to daytime feeding in otherwise nocturnally active mice was thought to be the biosynthesis of ketone bodies in the liver, influenced by the molecular clock gene *Per2*. In order to confirm this, we created mice with tissue or cell-type specific knockout of the monocarboxylate transporter 1, which transports ketone bodies. This allowed us to confirm that liver metabolism and secretion of ketone bodies via monocarboxylate transporter 1 affect the adaptation to feeding time.
In a parallel study, we found that the manic behaviour of mice that results from total-body mutation of the molecular clock gene *Per2* can be replicated by glial *Per2* knockout. Furthermore, the knockout of *Per2* from a specific brain region, the nucleus accumbens, is sufficient to reduce the despair perception in the mice. This new model for studying manic-depressive behaviour led us to the identification of potential candidate genes that could affect such changes, the GABA transporter 2 and dopamine receptor D3.
Our two parallel studies looked at different time-dependent behaviours, but in both cases tissue and cell-type specific approaches were used to answer previous unknowns.

Jury:
Prof. Urs Albrecht (thesis supervisor)
Prof. Jörn Dengjel (internal co-examiner)
Prof. David Gatfield (external co-examiner)
Prof. Thomas Flatt (president of the jury)