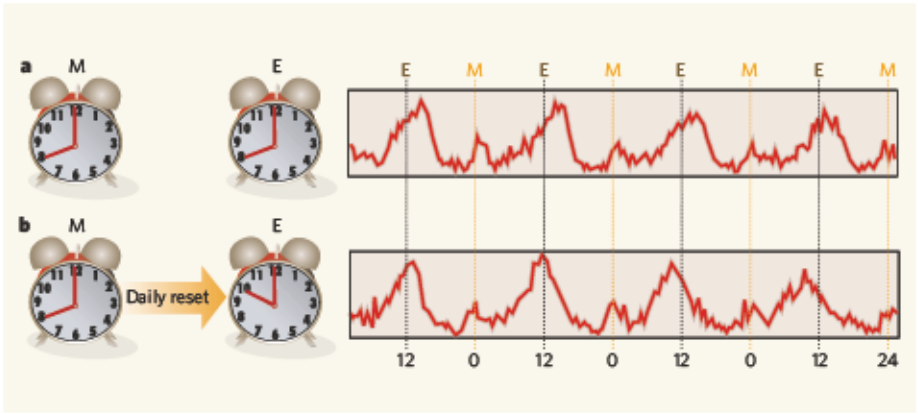

Figure 1 | Synchronization of fruitfly circadian oscillators. The oscillators in the fruitfly (*Drosophila melanogaster*) brain that control morning (M) and evening (E) peaks of locomotor activity reside in distinct neuronal cell populations. **a**, Under normal circumstances, the M and E oscillators run with the same intrinsic period. **b**, When the E oscillator is genetically modified to run with an intrinsic period shorter than that of the M oscillator, the evening peak of activity occurs earlier than usual. But the peak-to-peak period of the evening peak of activity is the same as that of the morning peak. This suggests that a signal is sent to the E oscillator once each day by the M oscillator to synchronize the phase of E to that of M, whereas in between these resets the E oscillator runs with its intrinsic period.

even in free-running DD conditions, the morning and evening peaks maintain a constant phase relationship with each other. So there must be some mechanism for keeping that relationship even in the absence of any environmental cues.

Stoleru *et al.* tackled this mechanism in their new paper[3]. The first question they addressed is whether there is a master–slave relationship between the M and E oscillators, or whether these oscillators mutually influence each other to collaboratively arrive at a constant phase relationship. To do so, the authors created genetically modified fruitflies in which the M and E oscillators run with intrinsic periods that differ by three to four hours. They found that, under free-running DD conditions, the period of behavioural locomotor activity is always determined by the intrinsic period of the M oscillator, suggesting that there is a master–slave relationship and that M is the master.

Moving to the cellular level, Stoleru *et al.* determined the period of the clock in M and E oscillator cells using a molecular marker. As would be expected if M is the master and E the slave, the period of clock oscillation in the E cells was determined by that of the M cells, and not by the intrinsic period of the E cells themselves.

So how does M exercise control? One possibility is that it exerts a continuous drive on E such that cellular oscillations in E track those of M on an hour-by-hour basis. Alternatively, it could be that E free-runs with its intrinsic period but is reset once a day by M so that its overall period is the same as M's.

To distinguish between these possibilities, Stoleru *et al.*[3] compared the phase of the evening peak of locomotor activity in fruitflies in which E had a genetically induced short intrinsic period and a normal M, with that in fruitflies with E and M both of normal period. The result was that fruitflies in which E runs fast exhibit their evening peak of activity about two hours earlier than normal fruitflies (Fig. 1). However, the overall peak-to-peak period of E is the same as that of M, suggesting that the M oscillator resets the E oscillator once a day. In between these resets E free-runs with its own faster intrinsic period.

Research does not end here, of course. Most obviously there is the issue of the resetting signal that M sends to E, and here one can speculate about the involvement of a neuropeptide called pigment-dispersing factor (PDF). M cells express PDF, and, in the absence of PDF signalling, the evening peak in LD conditions occurs about two hours earlier than in normal fruitflies[6]. Moreover, the PDF receptor has recently been identified, and it is indeed expressed in at least some of the cells that comprise the E oscillator[7–9]. Closer to home, investigators will be naturally curious as to whether the M and E oscillators in the mammalian brain communicate in a similar fashion to those in the fruitfly. It is to be expected that future work will resolve these and other fascinating questions raised by Stoleru and colleagues' findings. ■

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1. Stoleru, D., Peng, Y., Agosto, J. & Rosbash, M. *Nature* **431**, 862–868 (2004).
2. Grima, B., Chelot, E., Xia, R. & Rouyer, F. *Nature* **431**, 869–873 (2004).
3. Stoleru, D., Peng, Y., Nawathean, P. & Rosbash, M. *Nature* **438**, 238–242 (2005).
4. Pittendrigh, C. S. & Daan, S. *J. Comp. Physiol.* **106**, 333–355 (1976).
5. Jagota, A., de la Iglesia, H. O. & Schwartz, W. J. *Nature Neurosci.* **3**, 372–376 (2000).
6. Renn, S. C., Park, J. H., Rosbash, M., Hall, J. C. & Taghert, P. H. *Cell* **99**, 791–802 (1999).
7. Mertens, I. *et al. Neuron* **48**, 213–219 (2005).
8. Lear, B. C. *et al. Neuron* **48**, 221–227 (2005).
9. Hyun, S. *et al. Neuron* **48**, 267–278 (2005).

50 YEARS AGO

"New Records in Human Power" — When testing the Swedish national ski-team for physical condition...values for oxygen intake as high as 6.1 l./min. were estimated. As these figures far surpassed the earlier maximum, it was of great interest to obtain direct measurements of those subjects' aerobic capacity... values are included from an investigation of capacity for hard muscular work of eighty-six healthy, well-trained students of physical education... The most striking difference between those students, on one hand, and the middle-distance runners and skiers, on the other, is found when comparing the capacity for oxygen uptake. Values for vital capacity, maximum heart-rate, pulmonary ventilation and concentration of blood lactic acid were of the same order. It is probable that a high aerobic capacity is an essential characteristic of people with a high standard of physical fitness with regard to endurance.
From *Nature* 12 November 1955.

100 YEARS AGO

Science scholars selected from the whole of Great Britain for their ability and promise, maintaining themselves on 17*s*. 9*d*. per week, were this year saved from much privation by secret gifts of small bursaries — see subjoined audited account. I have no right to ask for help from the generous men who helped me last year, but I have all the sturdiness of a chartered beggar — I ask in a good cause.

It was originally intended that these bursaries should be given only to such National Scholars as required assistance, but some of the subscribers have given me power to assist other students of the college. Also one of the two City Companies has given me power to grant an occasional bursary of more than ten pounds. It is understood that every student is morally bound to repay this money to the fund at some future time. John Perry
From *Nature* 9 November 1905.

50 & 100 YEARS AGO