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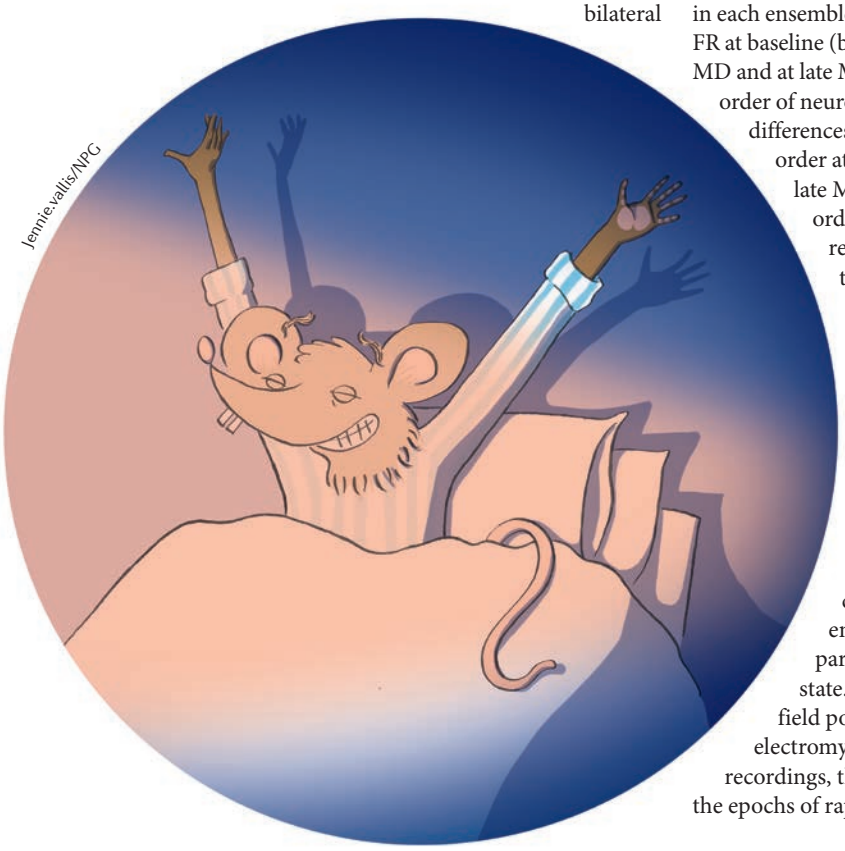
CORTICAL PHYSIOLOGY

Waking up homeostasis

> FR recovery was greater in the extended periods of waking than during the shorter, natural bouts

Homeostatic mechanisms are thought to maintain overall levels of activity within a cortical network within a narrow range. However, how the 'set point' of firing activity is determined and whether homeostatic mechanisms occur continually or during specific behavioural states such as during wake or sleep is not clear. In a new paper in *Cell*, Turrigiano and colleagues show that the diminished firing rates (FRs) of input-deprived cortical neurons return to a cell-specific baseline over a number of days, and that the restoration of these FRs takes place primarily while the animal is awake.

The authors implanted electrodes to record the activity of individual neurons in the bilateral primary visual cortex (V1) of rats, starting on postnatal day 24 (P24). Monocular deprivation (MD; achieved by suturing one eye closed) beginning on P26 led to a marked drop in FRs of individual neurons in the contralateral V1 by P28 (early MD), but these FRs then gradually returned to within 15% of their baseline levels by P31–P32 (late MD). By contrast, FRs in the ipsilateral V1 remained relatively stable over the full 9 days of recording.



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To establish whether the FR of each neuron returned to its own individual set point, or whether each ensemble had a general set point of activity, the authors tracked the firing of individual deprived V1 neurons over the 9 days. They ranked neurons in each ensemble according to their FR at baseline (before MD), at early MD and at late MD. The ranked order of neurons exhibited many differences from the baseline order at early MD but, by late MD, the baseline order had been largely restored. This implies that each neuron has its own FR set point to which it returns after perturbation.

Next, the authors set out to determine whether the restoration of the FR of each deprived neuron happened continually or was enriched during a particular behavioural state. By analysing local field potential (LFP), electromyogram and video recordings, the authors tracked the epochs of rapid eye movement (REM) sleep, non-REM sleep, quiet wake or active wake of each animal during the 'rebound period' of MD — that is, between early MD and late MD — and extracted FR data for each epoch of each state. Strikingly, they found that, whereas the FRs of individual deprived neurons stayed stable during REM-sleep, non-REM-sleep and quiet-wake epochs, they increased during active-wake epochs within the rebound period. Thus, FR homeostasis in response to MD occurs selectively during active wake.

Interestingly, longer active-wake epochs were associated with larger increases in the rebounding FRs of deprived neurons. To directly test this association, the authors gently handled the rats to artificially extend the duration of alternate spontaneous active-wake epochs to 1 hour over the course of 24 hours during the rebound period. Indeed, the amount of FR recovery was greater in the extended periods of waking than during the shorter, natural bouts. Moreover, FRs rebounded to a larger extent during 'wake-dense' periods (that is, 4-hour periods naturally containing more than 65% wake) than during sleep-dense periods. Thus, FR homeostasis returns increasingly with time spent actively awake.

This study has two main conclusions: first, individual neurons have their own FR set points around which their activity is maintained; and, second, the resetting of FRs to their baseline occurs during active waking.

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ORIGINAL ARTICLE Hengen, K. B. *et al.* Neuronal firing rate homeostasis is inhibited by sleep and promoted by wake. *Cell* **165**, 180–191 (2016)