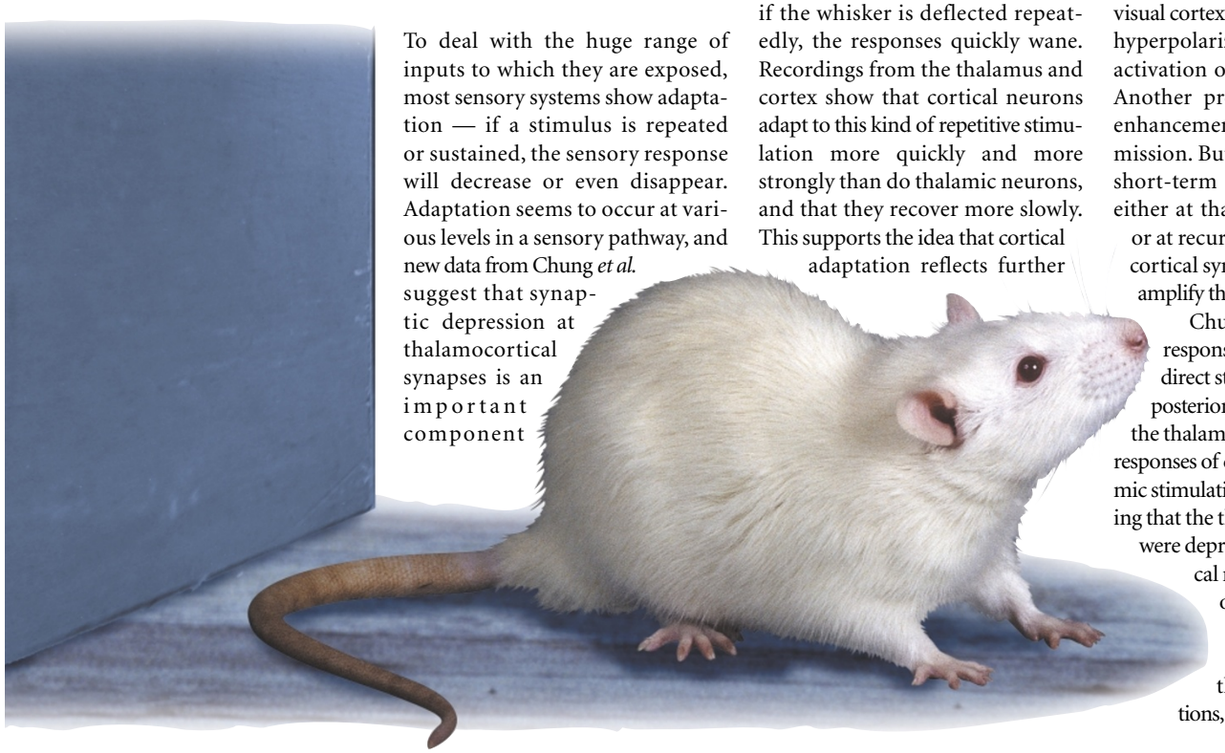
SENSORY SYSTEMS

Fast adaptors



To deal with the huge range of inputs to which they are exposed, most sensory systems show adaptation — if a stimulus is repeated or sustained, the sensory response will decrease or even disappear. Adaptation seems to occur at various levels in a sensory pathway, and new data from Chung *et al.* suggest that synaptic depression at thalamocortical synapses is an important component of this process, at least in the somatosensory system.

When a rat's whisker is deflected, neurons in the somatosensory thalamus and cortex fire strongly. But if the whisker is deflected repeatedly, the responses quickly wane. Recordings from the thalamus and cortex show that cortical neurons adapt to this kind of repetitive stimulation more quickly and more strongly than do thalamic neurons, and that they recover more slowly. This supports the idea that cortical adaptation reflects further processes, over and above those that lead to thalamic adaptation.

There are several possible mechanisms of cortical adaptation. For example, slower adaptation in the cat visual cortex results from membrane hyperpolarization, probably due to activation of a potassium current. Another proposed mechanism is enhancement of inhibitory transmission. But a leading candidate is short-term synaptic depression, either at thalamocortical synapses or at recurrent excitatory cortico-cortical synapses (which normally amplify the signal).

Chung *et al.* recorded the responses of cortical neurons to direct stimulation of the ventroposteriomedial nucleus (VPM) of the thalamus. After adaptation, the responses of cortical neurons to thalamic stimulation were smaller, indicating that the thalamocortical synapses were depressed. By contrast, cortical responses to stimulation of other cortical neurons did not decrease after adaptation, indicating that, under these conditions, recurrent cortico-cortical

CIRCADIAN RHYTHMS

Peripheral wheels and pinions

Circadian rhythms have been identified not only in the brain but also in peripheral organs. How do the central and peripheral clocks interact? Two recent studies that compare circadian gene expression in brain, liver and heart provide us with new clues about their possible relationship.

Our early thinking on circadian rhythmicity was guided by the idea that a central clock — the suprachiasmatic nucleus (SCN) of the hypothalamus — governed our sleep–wake cycles. The subsequent identification of genes with circadian expression patterns in the SCN began to clarify how this brain region might do its job and, at the same time, led to the discovery of circadian clocks in peripheral tissues. This finding prompted a new fundamental question that has begun to be addressed — how do the different clocks interact to control rhythmicity on a global scale? To answer this question, it might be helpful to know the similarities and differences between the circadian patterns of gene expression in different organs. The two new papers shed light on this issue.

Using microarrays, Panda *et al.* compared circadian gene expression between the SCN and the liver. They identified several hundred cycling transcripts, the products of which regulate key functions of both organs. Remarkably, they found that the peaks of expression of the different transcripts were distributed throughout the circadian cycle, and that most of the transcripts were specific to the SCN or the liver. Storch *et al.* made a similar comparison between liver and heart, which led them to identify a wide variety of genes with analogous, out-of-phase patterns of circadian expression. Similar to the findings of Panda and colleagues, Storch *et al.* found that most of the identified genes showed circadian expression in liver or heart, but not in both. However, tissue-specific gene expression could not account for the differences in this case, as most of the transcripts were present in both organs.

Both studies converge on the idea that many key processes are under circadian control throughout the organism, and give us a glimpse of how the different wheels of the clock might work together. Although many of the transcripts differ from organ to organ, the cycling expression of others, such as some genes of the core circadian oscillator, is conserved across different organs. Do they connect the central pinion and the peripheral wheels? Some of the cycling transcripts are candidates for new clock genes or might be responsive to circulating factors that show circadian rhythmicity. How is their expression controlled? This is just the preamble to the instructions on how to build the whole clock.

Juan Carlos López

References and links

ORIGINAL RESEARCH PAPERS Panda, S. *et al.* Coordinated transcription of key pathways in the mouse by the circadian *Clock*. *Cell* **109**, 307–320 (2002) | Storch, K.-F. *et al.* Extensive and divergent circadian gene expression in liver and heart. *Nature* **417**, 78–83 (2002)

FURTHER READING Buijs, R. M. & Kalsbeek, A. Hypothalamic integration of central and peripheral clocks. *Nature Rev. Neurosci.* **2**, 521–526 (2001) | Young, M. W. & Kay, S. A. Time zones: a comparative genetics of circadian clocks. *Nature Rev. Genet.* **2**, 702–715 (2001)

WEB SITES

Encyclopedia of Life Sciences: http://www.els.net/circadian rhythms

synapses do not become depressed. The authors suggest that this lack of depression might be observed because the cortical neurons respond to only the first few stimuli in a train (owing to thalamocortical depression), so their synapses have time to recover during the rest of the train.

Further recordings ruled out other potential mechanisms of adaptation. The cortical cells showed no changes in membrane potential, input resistance or membrane excitability following adaptation, indicating that such postsynaptic effects are unlikely to account for rapid adaptation in this system. This contrasts with the previous finding that slower adaptation in the visual system results from membrane hyperpolarization in the cortex, and may represent a general difference between fast and slow adaptation.

Rachel Jones

References and links

ORIGINAL RESEARCH PAPER Chung, S. *et al.* Short-term depression at thalamocortical synapses contributes to rapid adaptation of cortical sensory responses *in vivo*. *Neuron* **34**, 437–446 (2002)

FURTHER READING Carandini, M. & Ferster, D. A tonic hyperpolarizaton underlying contrast adaptation in cat visual cortex. *Science* **276**, 949–952 (1997)

DEVELOPMENT

Sorted!

An important process in the organization of the developing nervous system is the clustering of neurons with similar properties to form nuclei. In a new study reported in *Cell*, Price *et al.* have examined how motor neurons in the spinal cord sort themselves into 'motor pools' — collections of neurons that innervate a common muscle target. It was already known that each motor pool expresses a distinct combination of transcription factors, but here the authors turned their attention to cell-surface molecules that might enable neurons of the same motor pool to recognize one another. Their results indicate an important role for adhesion molecules of the type II cadherin family.

Price *et al.* cloned 15 different cadherins from the chick embryo spinal cord, and they examined their expression patterns at the lumbar level, where the motor pools have been best characterized. They found that most motor pools express more than one cadherin gene, and each expresses a different combination of type II cadherins. This pattern is achieved through two mechanisms: some genes, such as *MN-cad*, *cad-12* and *cad-8*, are initially expressed in most or all motor neurons and are subsequently downregulated in certain pools, whereas others, such as *T-cad*, *cad-6b* and *cad-7*, are activated in a fraction of motor neurons after they have left the cell cycle. The emergence of these expression patterns coincides with the time when the neurons are beginning to segregate, making the cadherins good candidates for driving this segregation.

The authors looked at the development of two motor pools, eF and A, which differ in the expression of a single type II cadherin (A expresses *MN-cad*, but eF does not). They generated mosaic embryos in which *MN-cad* was either expressed ectopically or inactivated in a random selection of cells. Both manipulations led to increased intermingling of eF and A neurons, indicating that MN-cad is important for the segregation of neurons between these two motor pools.

They also showed that misexpression of the transcription factor Er81 causes ectopic expression of *MN-cad*, raising the possibility that the transcriptional profile of motor neurons translates into a cadherin 'code' on the cell surface. So, although this research is still at an early stage, the type II cadherins are already emerging as a possible link between transcription-factor expression and neuronal surface properties in motor pools.

Heather Wood

References and links

ORIGINAL RESEARCH PAPER Price, S. R. *et al.* Regulation of motor neuron pool sorting by differential expression of type II cadherins. *Cell* **109**, 205–216 (2002)

FURTHER READING Jessell, T. M. Neuronal specification in the spinal cord: inductive signals and transcriptional codes. *Nature Rev. Genet.* **1**, 20–29 (2000)