GENES AND BEHAVIOUR

Live fast, die young

Sleep deprivation, as any new parent or college student can attest, leads to considerable impairments in behaviour. Even fruitflies need to sleep, but a study published in *Nature* shows that a mutation in a potassium channel can allow them to function normally on just a third as much sleep as wild-type flies.

Clearly, sleep serves some essential function, in species from humans to *Drosophila melanogaster*. Remarkably, however, it remains unknown what this function is, or how sleep is homeostatically controlled so that the pressure to sleep increases with time awake.

The study by Cirelli and colleagues describes a mutant line of *D. melanogaster* named *minisleep* (*mns*). These flies sleep for only about one-third of the duration for which wild-type flies sleep (4–5 h compared with 9–15 h). Despite this dramatic reduction in the length of each sleep episode, the number of bouts of sleep and general periodic locomotor activity were similar to those of wild-type flies. The authors conclude that the mutation does not influence the circadian clock system, which ensures that animals sleep at appropriate times.

Surprisingly, the mutant flies seem to behave normally despite this lack of sleep, and, unlike their wild-type relatives, are not impaired by further sleep deprivation.

The mutation that leads to this unusual phenotype was found to be in a conserved region of the well-studied *Shaker* gene, which encodes a voltage-dependent potassium channel that is involved in membrane polarization and presynaptic transmitter release. Taking advantage of the powerful tools available in *D. melanogaster* genetics, the authors showed that the phenotype is specific to the *Shaker* locus and does not depend on genetic background. Furthermore, other ion channel mutations did not cause abnormal sleep phenotypes.

The results might pave the way for a greater understanding of how the need for sleep is measured and controlled, much as early genetic studies of *period* and other mutations in *D. melanogaster* led to an understanding of the circadian clock. Clearly this is just the beginning of

NEUROGENESIS

Nervous beginnings

Although proneural genes are known to regulate the differentiation, position and identity of neurons during the early development of a wide range of organisms — from flies to humans — it is unclear which genes lie immediately downstream of them. A series of experiments using transgenic mice, reported in *Development*, show, for the first time, a conclusive link between a proneural gene and its direct target, and the authors link this interaction to a specific neuronal fate.

Proneural genes encode basic helix–loop–helix (bHLH) proteins, which activate transcription by binding to the E-box regulatory sequence of their target gene. In the developing spinal cord of the mouse, cells adjacent to the roof plate express the proneural gene *Math1* and also a Bar-class homeobox gene *Mbh1*. Previous work has shown that *Math1* is involved in controlling the number of dI1 cells and commissural neurons, that dI1 cells express *Mbh1*, and that *Mbh1*-positive cells give rise to commissural neurons. However, until now, the functional relationship between the two genes and their influence on neuronal cell fate was unclear. Now Saba and colleagues have shown that *Mbh1* is a direct downstream target of MATH1 and that MBH1 confers commissural neural identity in the spinal cord.

Using a series of deletions and a *LacZ* reporter gene, the authors discovered that the *Mbh1* enhancer contains an E-box that is well conserved among mice, rats and humans, and showed that a mutation known to disrupt the binding of MATH1 to this site abolishes *Mbh1* expression. This proved that *Mbh1* expression in the dorsal spinal cord requires an E-box, as might be expected if MATH1 binds directly to regulate *Mbh1* expression. The relationship between *Mbh1* and MATH1, which was indicated by other studies, was then confirmed by knockout and overexpression studies. *Mbh1* expression was absent from *Math1*-knockout embryos, and expressing MATH1 on the sides of the dorsal cord led to the ectopic expression of *Mbh1* in these regions.

Biochemical assays reinforced the conclusion drawn from the *in vivo* experiments. An anti-MATH1 antibody specifically immunoprecipitated *Mbh1* enhancer DNA fragments that contain the E-box, thereby showing that endogenous MATH1 bound the enhancer at the binding site. Similar results were obtained for misexpressed MATH1. But what does *Mbh1* do? Evidence obtained from chimaeric proteins of MBH1 showed that the protein requires a transcriptional-activator domain to inhibit the generation of commissural neurons by MATH1, which indicates that MBH1 is a transcriptional repressor.

This is the first demonstration that an aspect of neuronal identity is determined immediately downstream of a bHLH protein, and reveals a chain of events leading to specific commissural neural identity in the spinal cord.

David Stevens

References and links

ORIGINAL RESEARCH PAPER Saba, R. *et al*. Commissural neuron identity is specified by a homeodomain protein, Mbh1, that is directly downstream of Math1. *Development* **132**, 2147–2155 (2005).

an interesting story. Do mutant flies simply need less sleep, or do they sleep more efficiently? Are the effects central or peripheral? It will also be important to determine whether the results are relevant to mammalian sleep regulation. Cirelli *et al*. suggest that this might be the case, on the basis of evidence that potassium channels are involved in mammalian sleep rhythms. In addition, some tantalizing hints come from a rare autoimmune disorder, Morvan's syndrome, in which sleeplessness might be associated with autoantibodies against voltage-dependent potassium channels.

There is one crucial caveat for anyone who reads this paper with hopes of a drug that could lead to a reduced need for sleep: compared with controls, the mutant flies had reduced lifespans.

John Spiro, Senior Editor, Nature

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VISUAL PROCESSING

Seeing all the angles

Two recent papers extend our understanding of the potential of functional imaging by showing that functional MRI (fMRI) images of activity in the earliest stages of visual cortex can be used to identify what a person is looking at.

Kamitani and Tong used fMRI to scan people's brains while they were looking at stimuli that consisted of lines in one of eight possible orientations. In monkeys, neurons in the primary visual cortex are arranged in 'orientation columns' that respond most strongly to a particular line orientation. However, these columns are too small to image reliably using fMRI. So, rather than trying to view the activity in individual orientation columns in the human visual cortex, the authors investigated whether each 'voxel' — the smallest subdivision of the image in an fMRI scan — showed orientation-dependent changes in activity, and whether these could be used to predict the orientation of the stimulus being viewed by a participant during a scan.

By applying linear pattern analysis techniques, the authors found that they could use fMRI scans to identify which of the eight orientations was being viewed. They then went on to investigate whether this ability to identify a person's 'brain state' could be extended to determine their mental state — a kind of 'mind-reading'. Participants viewed a pattern that consisted of two overlapping orientation stimuli, and had to pay attention to one orientation while ignoring the other. fMRI scans of the early visual cortical areas V1 and V2 taken during these trials could be used to predict which orientation a participant was concentrating on, showing that the information in the fMRI scans relates not only to the objective nature of the visual stimulus, but also to the subjective experience of the person who is being scanned.

Haynes and Rees also showed that fMRI scans could be used to predict which orientation a person was viewing. They took this further by investigating the effects of 'invisible' stimuli — images that are 'masked' by other stimuli so that the participant is not aware of seeing them. Such stimuli can cause 'interference' effects in psychophysical studies, showing that they are influencing visual processing in some way. Haynes and Rees found that their fMRI scans of cortical area V1 could be used to predict the orientation of such a masked stimulus, even though the subject didn't consciously see it.

As well as showing the ability of fMRI scans to extract information about visual processing in the early visual cortex, these two studies provide insights into the importance of V1 and V2 for conscious visual perception. On the one hand, activity in V1 and V2 reflects the subjective experience of a person who is paying attention to one of two simultaneously presented stimuli; whereas on the other hand, masked stimuli produce activity changes in V1 that are clearly not sufficient to allow perception of the stimulus. Further studies of this type should advance our understanding of how activity in the brain relates to conscious experience.

Rachel Jones

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