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Sleepless times

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Everyone knows what it feels like to lack sleep. The usual drive to get on with life is diminished. Problems are difficult to cope with. The urge to do any physical exercise is low. Short temper is just around the corner and the desire for a nap becomes greater as the hours tick by. Intuitively, everyone knows that you need to sleep to recharge the battery. It sounds simple enough because we know we feel restored after some rest and we've been living with it ever since we were born. But – like any physiological process – the act of sleeping is not so straightforward. Something inside us has to tell us: 'it's time to sleep'. And something else has to say: 'you need to sleep'. Our quality of sleep is driven by these two notions. Since the 1960s, scientists have been searching for genes which are at the heart of such processes. Recently, one protein named 'Sleepless' was discovered. Sleepless seems to be directly involved in telling us that all activity is to be put on hold for the space of a rest.

Even a fly has a soul

Michelle Charles, 2006

That processes such as memory, learning and sleep could have a genetic basis was still inconceivable for many in the 1960s, an epoch which saw the birth of 'neurogenetics' – a field of biology which strains to demonstrate that there are behaviours which are directly linked to genes. Almost fifty years later, there are not many scientists who would argue the contrary… Perhaps one of the best arguments is that we now know of the existence of genetic diseases linked to behavioural disorders. Alzheimer[i] is one. The Savant Syndrome[ii] is a second. And narcolepsy[iii] is another.

Drosophila has been a great model organism for such fields of research. However, as far as sleep goes, scientists were not persuaded that flies actually had that need. In the past decades, sleep has been defined according to electroencephalogram (EEG) patterns recorded in vertebrate brains. But it is not an easy task to measure EEG patterns in a fly… This said, there are moments in the day when a fly's activity is markedly reduced. And that is at night – just like humans. So, scientists have reverted to a theory which prevailed before the advent of EEGs: a resting animal is an animal which remains still and is difficult to rouse. In this light, *Drosophila* seems to have the same resting needs as humans: it sleeps overnight, and is happy to have a snooze in the mid-afternoon.

The act of sleeping is driven by two views: there is a time to sleep and a need to sleep. Roughly, the time to sleep is defined by the 24 hour cycle we all know. And the need to sleep is defined by all these sensations we gather towards the end of a day, or after a restless night and that we call 'feeling tired'. We all know that feeling. But what is happening on the molecular level? What is it inside us that is triggering off the need-to-sleep signals? Well, the Sleepless protein may have something to do with it. This protein is a GPI-anchored membrane protein enriched in the brain. Sleepless could be a signal-inducing protein, which fires off signals to the brain. What kind of signals?

It really all depends on how you define what 'sleep' is. One theory is that sleep helps restore energy lost whilst awake. From the point of view of logistics, a sleeping individual slips into a 'living form' which is not only out of order but also – hopefully – out of danger because it is incapable of reaction. Another theory is that sleep is used to re-arrange the many synapses which are created on a daily basis. If all these synapses were kept, our brains would fast become overcrowded and would not be able to house them all. Consequently, sleep could be seen as taking the brain offline for a time, with a view to re-organise for spatial and quality reasons.

Where does Sleepless come in? It has been shown for some time now that the process of sleep seems to be dependent on neuron membrane excitability. The neuron excitability of a resting person is lowered – whereas a person who is fully awake shows an increased membrane excitability. It seems that Sleepless has a direct effect on this excitability. Indeed, Sleepless may well send out signals to membrane potassium channels which can control a membrane's excitability by either increasing it, or reducing it. Certainly, when Sleepless is defective, no signal is sent out. As a consequence, neuron excitability is not reduced and flies can sleep up to 80% less than their wild-type kin! This would demonstrate that the control of neuron excitability is a prerequisite for sleep.

Problems revolving around sleep, such as insomnia, are part of our modern society. If scientists achieve a greater understanding on the molecular level of what sleep is then – theoretically – they should be able to design drugs which could either help us to sleep better of even prevent us from sleeping – something any student swatting for exams has felt the need for, or bus drivers who do long hours of driving for instance. Nothing which should be encouraged but where there is money to be made, there is a market. Scientists are even thinking of going a notch further. What if other forms of behaviour – such as common sense, jealousy or altruism – were genetically controlled? Nonsense? 50 years ago, no-one thought that there could have been a genetic component to sleep. This said, there is still a long way to go. Can the sleep of an insect compare to that of a human? Do insects dream for example? And how do you measure the common sense of a fly?

Cross-references to Swiss-Prot

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[i] « Tangled », Protein Spotlight issue 83

[ii] « The things we forget », Protein Spotlight issue 32

[iii] « Qui dort dîne », Protein Spotlight issue 15