Light, Sleep and Time – and how they Interact by Professor Foster on 19th January 2018

Professor Foster said he would speak about Sleep and the Circadian Rhythm; disruption of the rhythm; the role of the Eyes; the effects of eye disease; and the development of suitable drugs.

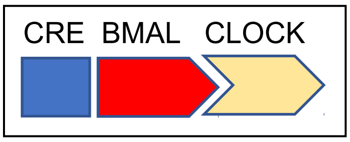
Eyes have to cope with illumination that changes from very low levels at night to high daytime levels: ranging from 0.01 to 100,000 lux. They have to work reliably over a wide temperature range. Domestic/office lighting is around 50 lux. In the animal world most hunting is done at dusk.

The core body temperature varies through the day, peaking in the mid-afternoon, with a minimum around 2am. After that it begins to rise in preparation for the next day – one often wakes up before dawn. During the morning it continues to rise (the danger period for stoke). Alertness picks up quickly in the morning, stays steady during the day but dips after 10pm - without one being aware of its decline – so don't have alcohol, a sedative, then drive home late at night. The desire for food is reduced at night. The immune system is less active at night. Other body functions have their rhythms too.

During sleep the brain processes information gained during the day (integrating it with previous memories and discarding dross). Professor Foster thought that dreams resulted from this and that they had no intrinsic value; however, on the emotional side enjoyable memories tend to be lost if one is tired, while bad memories are kept. Even without modern knowledge, writers – eg Shakespeare - have always praised the value of sleep.

The whole brain clears waste metabolites and refurbishes itself at night. On average we sleep for 36% of our lives. The homeostatic sleep drive, brought on by a daily build-up of adenosine (a by-product of energy consumption by cells) in the brain, produces increasing tiredness – though this is blocked by caffeine – and can be overridden by the Circadian clock.

This is generated in a pair of Suprachiasmatic nuclei (SCN) in the hypothalamus, immediately above (supra), and either side of, the optic 'chiasm', where the optic nerves from the two eyes cross. The two nuclei together produce the Circadian (circa = about, dia = day) rhythm. This clock signal is propagated through the body and regulates the clocks of other body functions.



Each nucleus has a number of identical clock cells, with a clock mechanism centred on a three-part structure shown in the diagram at the right: the CLOCK is driven by BMAL, both elements with feedback loops to control the output. The CRE has its own set of receptors in the retina and controls BMAL.

Unlike the visual cortex, which rapidly responds to signals from the retina, the SCN slowly responds to light/dark intensity changes. The CRE's receptor is in the retina but not among the rods and cones, instead being in the nerve ganglion beyond. (You will recall that the active part of the retina is at the back, light passing through the ganglion to reach it.) After many decades of studying eye function, the visual establishment had difficulty in accepting that there was another receptor in the eye.

Eventually Professor Foster found it. Blind people, whether being born blind or through accident, can tell night from day - but not if they are blindfolded - there had to be a receptor in the eye. Studies on mutant mice gave similar results. Studies on fish which have to cope with very low light levels below the water surface, showed that they had receptors on their skin as well as in their eyes. This gave a clue as to where the light/dark detector might be in the eye. Its slow response and unexpected location had kept it hidden. This receptor responds to a blue wavelength of 480nm, and needs a quite bright 3000 lux.

One consequence of the ignorance of this receptor was that blind people could be encouraged to have their 'useless' eyes, which could still be prone to disease, replaced with artificial ones.

Disruption of the circadian rhythm comes with modern life. Edison's mass production of the electric lamp started the rot. We can stay up later, but equally we can spend hours in poorly lit homes and offices with insufficient light for the eyes to raise alertness. Caffeine, however, raises alertness and lasts 5 to 9 hours.

Disruption impairs the regulation of other clocks in the body and synchronism is lost. Crossing one time zone in a day does no harm, but more than that can bring on jet lag. Bodily clock regulation is not helped by sedatives such as alcohol or travel pills.

Short term disruption can cause: loss of attention - microsleeps (very short but uncontrollable) - a failure to process information or remember things - reduced cognition and creativity.

Long term disruption, caused for instance by shift work, can have more serious consequences for one's health:

- supressed immunity – cancer – diabetes – dementia – Alzheimer's disease.

Knowledge of how the CRE works gives an opening for drug development for conditions in which interfere with circadian control.

During the talk Professor Foster said that although fish and other animals may have extra-ocular light sensors, this is not the case for mammals whose only visual receptors are in their eyes. Arctic reindeer, with months of darkness followed by months of daylight have no circadian rhythm - they just keep going continuously.