Neurons and biological timing

https://neurodegenerationresearch.eu/survey/neurons-and-biological-timing/

Title of project or programme

Neurons and biological timing

Principal Investigators of project/programme grant

Title	Forname	Surname	Institution	Country
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- United Kingdom

Source of funding information

Medical Research Council

Total sum awarded (Euro)

4993803.28

Start date of award

01-04-2005

Total duration of award in months

60

The project/programme is most relevant to

- Alzheimer’s disease and other dementias
- Huntington’s disease

Keywords

Body clock, circadian, suprachiasmatic nuclei, Alzheimer’s disease, Huntington’s disease, corticosteroids, sleep, biological rhythms

Research abstract in English

The current model of the circadian oscillator within the suprachiasmatic nucleus (SCN) is one of

interlocked transcriptional/post-translational feedback loops, which sustain autonomous 24 h cycles of gene expression. Notwithstanding its success, the model is heavily based on evidence and inferences of the properties and behaviour of clock factors in contexts far removed from the SCN. Our objective is to conduct a series of definitive experiments to test the predictions of the model in the context of the SCN neuronal environment, the principal neural oscillator. We shall exploit a combination of neurobiological, molecular genetic, biochemical and behavioural approaches, both in vitro and in vivo. Specifically, we aim to define the nature of dynamic interactions between oscillator components, both protein and DNA regulatory sequences, in the SCN. If the model is correct, it should be possible to control circadian phase, and indeed to stop and start the cycle at will, by temporally regulated expression of core components of the loop. The second aim of the work will be to elucidate the molecular and cellular mechanisms responsible for circadian regulation within the SCN neuron and SCN targets in the brain, and thence to peripheral, tissue-based clocks. Finally, with growing knowledge of circadian molecular neurobiology, it will be possible to explore the relevance of circadian timing to neurological disease, in particular by examining circadian function in animal models of such diseases, including Huntington’s disease (HD) and Alzheimer’s disease (AD)

Lay Summary

Common experience confirms the role of our daily (circadian) “body clock” in determining our abilities to act and to think and the daily changes in mood and how we feel. Conditions that affect the smooth operation of the body clock, such as shift-work, jet-lag and old-age, cause problems for the individual, and across Society are a major and growing cause of industrial accidents and disease. Loss of daily control to the sleep/wake cycle is a primary complaint of old-age and the commonest cause of referrals to nursing homes. The recent discovery of the genes that code for the circadian clockwork in the brain now makes it possible to unravel the cellular processes that sustain our daily cycles of physiology and behaviour. The aim of this project is to examine the core clock mechanism of the brain’s principal circadian clock, the suprachiasmatic nucleus (SCN). We shall examine the interplay between the different “clock” proteins, and how they control the activity of their own and other “clock” genes, in order that the activity of the brain and the body changes in a predictable and very regular way over the course of day and night.