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CIRCADIAN RHYTHMS

Cycling vesicles for a cycling SCN

The suprachiasmatic nucleus (SCN) in the hypothalamus controls the circadian rhythmicity of many physiological processes through clock genes that are expressed in a cyclical fashion. The products of these genes in turn regulate the daily expression of many other genes. Hastings and colleagues now report that circadian regulation can also occur at the post-transcriptional level, for example for SCN proteins associated with synaptic vesicle cycling. Moreover, they show that vesicle recycling has an important role in maintaining circadian clock gene expression in the SCN.

The authors extracted proteins from mouse SCN at different circadian time points and determined their levels using a proteomic approach. This revealed 53 'spots' (~6% of expressed proteins) showing clear changes in abundance between samples that were taken 12 hours apart. Some of these 53 proteins were isoforms, leaving 34 unique proteins identified that were under strong circadian control, including heat shock proteins, factors involved in cellular metabolism and factors involved in synaptic vesicle recycling.

The mRNAs encoding these proteins did not show circadian regulation, and these proteins had therefore not previously been recognized as being under clock control. This finding points to a role for post-transcriptional mechanisms in circadian regulation in the SCN, as had previously been shown in the liver.

The authors next investigated whether vesicle cycling has a functional role in pacemaking in the SCN. They treated organotypic SCN slices with either dynasore, which inhibits endocytosis, or botulinum toxin A (Botox A), which inhibits exocytosis, and measured the effect of these compounds on the expression of the clock gene Period 1 (*Per1*) and the clock protein Per2. Both treatments reduced the amplitude of *Per1* and Per2 cycling, and Botox A also lengthened the period of oscillation, demonstrating that impaired vesicle cycling disrupts pacemaking.

These findings show that the circadian regulation of proteins involved in vesicle cycling in the SCN can occur at a post-transcriptional level and suggest that vesicle cycling itself is a mechanism whereby the SCN sustains rhythmicity.

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ORIGINAL RESEARCH PAPER Deery, M. J. *et al.* Proteomic analysis reveals the role of synaptic vesicle cycling in sustaining the suprachiasmatic circadian clock. *Curr. Biol.* **19**, 1–6 (2009)

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