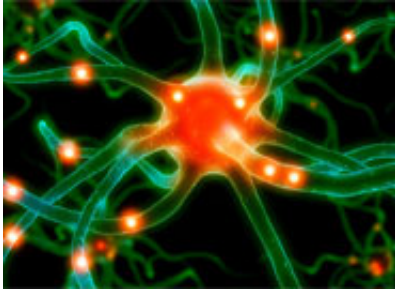


Hormones found to affect gene activity

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(PhysOrg.com) -- Intermittent signaling by steroid hormones can affect the way genes are expressed in rodents, according to research by scientists at the University of Bristol and the National Cancer Institute (NCI), USA. This work has major implications for understanding how steroids work and opens novel avenues for new therapies.

The findings are published online and will appear in the September 2009 issue of [Nature Cell Biology](#).

The release of hormones by the body's glands can occur in an episodic, or ultradian, pattern, which consists of repeated periods of release that take place throughout a 24-hour, or circadian, period. Glucocorticoid hormones, which were investigated in this study, are [steroid hormones](#) secreted by the adrenal glands that are involved in a large variety of animal and human physiological responses.

Glucocorticoids act through the glucocorticoid receptor, which is expressed in almost every cell in the body and regulates genes controlling development, [metabolism](#), and [immune response](#).

Studies of the glucocorticoid receptor typically assess gene responses after long-term stimulation with synthetic hormones. However, such treatments may not fully replicate the actual situation in living animals because, in addition to being released from the adrenal glands in a 24-hour circadian pattern, these hormones are also released in a pulsing mode, cycling approximately every hour, in what is referred to as ultradian cycling.

In this new study, the researchers demonstrate that ultradian [hormone](#) stimulation induces the pulsed expression of genes (known as gene pulsing) over the same period, both in cultured cells and in animal models. Initially, the researchers administered corticosterone, a naturally occurring glucocorticoid hormone in rodents, in a pulsed manner to cultured mouse cells and then observed that the levels of newly synthesized [RNA](#) from glucocorticoid receptor-regulated genes tracked precisely with the hormone pulses.

The reported research results argue that gene pulsing regulated by glucocorticoid receptors is directly linked to varying levels of gene activity. Professor Stafford Lightman, head of the Henry Wellcome Laboratories for Integrative Neuroscience and Endocrinology, at the University of Bristol, said: “We have previously shown that the hormone cortisol is released in pulses in man as well as rodents. The present results now show that this pattern of hormone release is critical for good health and provides a novel concept for new drug design.”

The researchers conclude that, considering the wide therapeutic use of glucocorticoids for arthritis and even some cancer indications, further studies to replicate their results and follow-up studies in humans are

clearly needed. Such studies will help to define the potential role of ultradian application of glucocorticoid receptor therapy.

More information: Stavreva,D.A., Wiench,M., John,S., Conway-Campbell,B.L., McKenna,M.A., Pooley,J.R., Johnson,T.A., Voss,T.C., Lightman,S.L., and Hager,G.L. Ultradian hormone stimulation induces glucocorticoid receptor-mediated pulses of gene transcription. [Nat. Cell Biol.](#) Online August 16, 2009. In print September 2009. Vol. 11, No. 9. Manuscript #NCB-H15221B.

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