

Expression profiling reveals circadian patterns of gene expression in the spinal sympathetic system: Focus on monoaminergic mechanisms.

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Circadian rhythms have rarely been described in the spinal cord. The intermediolateral nucleus (IML) of the thoraco-lumbar spinal cord is the site of preganglionic sympathetic neurons (SPNs) and it receives modulatory inputs from descending dopamine (DA) and serotonergic (5-HT) systems. A dysfunction in these projections to the IML is implicated in the circadian-related sleep disorder Restless Legs Syndrome (RLS).

Combining the technologies of fluorescent reporters, laser-capture microdissection and DNA microarrays we identified circadian changes in gene expression in the IML. Adult mice were kept under a 12/12 day-night light regime, and i.p. injected with fluorogold to label SPNs in the IML. Spinal cords were removed in 4 hr intervals beginning 1 hr prior to daytime. Captured mRNA from the IML was amplified and hybridized with Affymetrix U74AV2 Murine genome microarrays.

Overall expression levels of DA and 5-HT-related genes were low. Genes identified as present either had no or variable circadian patterns. Clear circadian rhythms with peaks at night were seen in the 5-HT receptors 5A, 7, 1D. Dopamine D4 (night peak) and D2 receptors (day peak) had opposite expression rhythms. Interestingly, proteins associated with transmitter synthesis, degradation and transport also underwent circadian variation with nighttime (DAT, DA-decarboxylase, tyrosine hydroxylase, ACh-ase) or daytime peaks (SERT, COMT). These unexpected findings suggest that either descending monoaminergic axon terminals express mRNA for these genes or that they are expressed by cells within the IML.

Regarding DA and 5-HT signaling pathways, we conclude that many but not all genes undergo circadian variation, with a correlated tendency for expression peaks during the animal's active period (night).

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