

The clockwork behind depression

Globally, an estimated 350 million people of all ages suffer from depression and the number is increasing. Currently, we don't know exactly what causes depression. However, what we do know is that depression and the circadian rhythm (? 24 h) are closely linked. Up to 80% of the depressed patients experience sleep disturbances and the sleep/wake cycle is the most important circadian rhythm of the body.

What exactly is a circadian rhythm? The word circadian mean “about a day”. Therefore, a circadian rhythm is any process in the body that follows a 24h cycle. For example, hormone secretion, cognition and even mood follow a rhythm over 24 h. All these processes are driven by the inner biological clock called the suprachiasmatic nucleus (SCN). The SCN consists of so-called clock genes that can be compared to the hands of a clock telling the body what time it is. Clock genes are not only limited to the biological clock in the brain since most cells of the body contain this clockwork machinery.

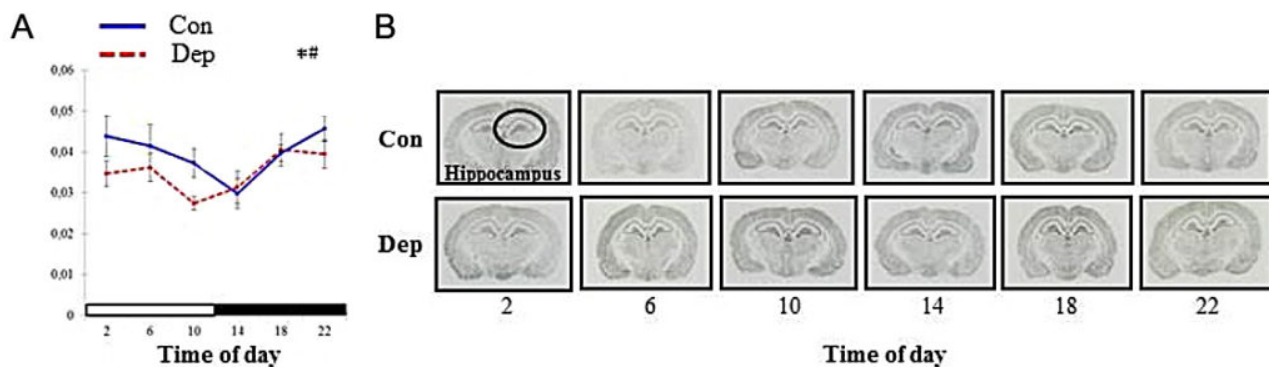


Fig. 1. A. The graph shows the 24 h expression pattern of the *Perl* clock gene in the hippocampus (center for memory and learning) after weeks of mild stress in the control group (con, blue) and in the depression-like group (Dep, red). B. Representative pictures of the rat specific gene (intense dark grey). The * indicates a circadian rhythm. The # tells us that the rhythm is different in depression-like rats compared to the control rats. Black bar indicates right.

In recent years the clockwork has been associated with disturbances of the circadian rhythm in depression.

The aim of the study was to investigate a potential connection between core clock genes (*Per1*, *Per2* and *Bmal1*) and a depression-like state using a rat model of depression. The rats were exposed to mild and chronic stressors to induce a depression-like behavior. Eight rats from the depression-like group and eight rats from a control group were sacrificed every 4 h during 24 h ($n_{\text{total}} = 96$). In order to explore the 24 h regulation of the clock genes, we took out the brain and cut

it in ultra-thin slides. The thin slides were stained to visualize the clock genes in different regions of the rat brain and afterwards indirectly measure the number of genes to compare.

We found that the response to stress was gene- and region-specific:

Per1 clock gene was primarily resistant to stress
Per2 and *Bmal1* were more easily disturbed by the stress

Furthermore, we demonstrated following:

The master clock/SCN was resistant to stressors (Fig. 1A)
Several other brain regions were affected indicated by an altered regulation of clock genes
The brain regions most affected by stress were regions controlling memory and learning as well as sleep and reward (Fig. 1B). All factors are well known to be involved depression

In conclusion:

Rats vulnerable to chronic, mild and unpredictable stress develop a depression-like state
Our study suggests that the depression-like state is likely associated with altered expression of clock genes in regions of the rat brain believed to be important for major depression

What can we learn from depression-like rats with an inner clock out of sync? We can learn that it is important to take good care of the circadian rhythm. How do we do that? The circadian rhythm likes routines. Thus, go to bed (not too late) the same time each day and get up the same time every morning, also in the weekend. Dampen the light in the evening and if you suffer from sleep disturbances be careful exposing yourself to light from the TV, iPhone or computer during the evening. In contrast, a lot of daylight in the morning hours helps you fall asleep in the evening and it has also been proposed to increase the quality of sleep.

Lastly, a little tip; following the circadian rhythm, the human brain has a peak in attention and focus around 10 a.m. which could be taken advantages of. Thus, perform the more difficult tasks in the morning and save the easier part of your work until the afternoon where the low point appears.

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Publication

[Altered Expression Pattern of Clock Genes in a Rat Model of Depression.](#)

Christiansen SL, Bouzinova EV, Fahrenkrug J, Wiborg O
Int J Neuropsychopharmacol. 2016 Dec 3