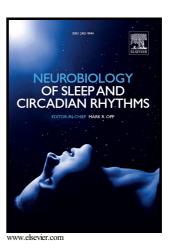
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ACCEPTED MANUSCRIPT

Sleep homeostasis and the circadian clock: Do the circadian pacemaker and the sleep homeostat influence each other's functioning?*

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Abstract

<u>Sleep is regulated by a homeostatic and a circadian process.</u> Together these two processes determine most aspects of sleep and related variables like sleepiness and alertness. The two processes are known to be able to work independently, but also to both influence sleep and sleep related variables in an additive or more complex manner. The question remains whether the two processes are directly influencing each other.

The present review summarizes evidence from behavioural and electroencephalographic determined sleep, electrophysiology, gene knock out mouse models, and mathematical modelling to explore whether sleep homeostasis can influence circadian clock functioning and *vice versa*.

There is a multitude of data available showing parallel action or influence of sleep homeostatic mechanisms and the circadian clock on several objective and subjective variables related to sleep and alertness. However, the evidence of a direct influence of the circadian clock on sleep homeostatic mechanisms is sparse and more research is needed, particularly applying longer sleep deprivations that include a second night.

The strongest evidence of an influence of sleep homeostatic mechanisms on clock functioning comes from sleep deprivation experiments, demonstrating an attenuation of

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