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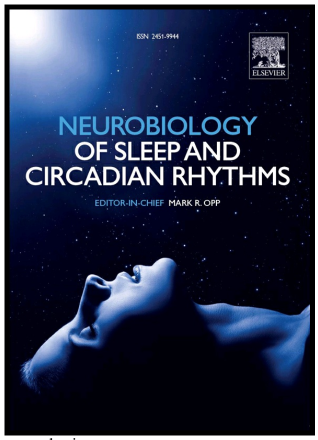

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Mathematical Modeling of Sleep State Dynamics in a Rodent Model of Shift Work

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Abstract

Millions of people worldwide are required to work when their physiology is tuned for sleep. By forcing wakefulness out of the body's normal schedule, shift workers face numerous adverse health consequences, including gastrointestinal problems, sleep problems, and higher rates of some diseases, including cancers. Recent studies have developed protocols to simulate shift work in rodents with the intention of assessing the effects of night shift work on subsequent sleep (Grønli et al., 2017). These studies have already provided important contributions to the understanding of the metabolic consequences of shift work (Arble et al., 2015; Marti et al., 2016; Opperhuizen, van Kerkhof, Proper, Rodenburg, & Kalsbeek, 2015) and sleep-wake-specific impacts of night-shift work (Grønli et al., 2017). However, our understanding of the causal mechanisms underlying night-shift-related sleep disturbances is limited. In order to advance toward a mechanistic understanding of sleep disruption in shift work, we model these data with two different approaches. First we apply a simple homeostatic model to quantify differences in the rates at which sleep need, as measured by slow wave activity during slow wave sleep (SWS) rises and falls. Second, we develop a simple and novel mathematical model of rodent sleep and use it to investigate the timing of sleep in a simulated shift work protocol (Grønli et al., 2017). This mathematical framework includes the circadian and homeostatic processes of the two process model, but additionally incorporates a stochastic process to model the polyphasic nature of rodent sleep. By changing only the time at which the rodents are forced to be awake, the model reproduces some key experimental results from the previous study, including correct proportions of time spent in each stage of sleep as a function of circadian time and the differences in total wake time and SWS bout durations in the rodents representing night-shift workers and those representing day-shift workers. Importantly, the model allows for deeper insight into circadian and homeostatic influences on sleep timing, as it demonstrates that the differences in SWS

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