



# Editorial: Sleep Deprivation, Circadian Misalignment and Addiction Vulnerability in Adolescents

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## Editorial on the Research Topic

### Sleep Deprivation, Circadian Misalignment and Addiction Vulnerability in Adolescents

Sleep is essential for almost all organisms, and it demonstrates a clear developmental trajectory in the amount of sleep needed from the early postnatal stage to adulthood (Hirshkowitz et al., 2015). The National Sleep Foundation of the United States of America recommends a minimum of ~8 h of daily sleep for adolescents (Hirshkowitz et al., 2015). However, a modern lifestyle involving excessive use of electronic devices, school/work, active social life, and late-night activities may have led to prevalent sleep problems including delayed sleep onset, shortened sleep duration, sleep fragmentation, and social jetlag in adolescents all around the world (Garipey et al., 2020; Wheaton and Claussen, 2021), which are further impacted by a stressful life event such as the COVID-19 pandemic (Becker et al., 2021). Adolescence is a critical developmental stage when the brain undergoes substantial circuit refinement and molecular changes important for its maturation (Casey et al., 2008; Moyer and Zuo, 2018; Faust et al., 2021). Thus, the adolescent brain is likely to be more vulnerable, compared to the adult brain, to sleep disturbances, circadian rhythm disruption, and associated substance abuse. This Research Topic highlights the developmental role of sleep and the interconnections of sleep regulation, circadian rhythm, and the neural circuits involved in addiction and reward-seeking behavior, and gathers several contributions, including three original research articles and a systematic review, from studies in different species using different approaches.

One of the articles of this Research Topic (Hasler et al.) reported a human study in 31 late adolescent females (18–22 y/o) assessing the neural response to monetary reward in correlation with the circadian alignment of sleep and weekend drinking. The authors showed that greater circadian misalignment prior to the weekend, assessed via the dim light melatonin onset (DLMO), was associated with lower neural responses in the mesocorticolimbic reward pathway to anticipated reward as measured by functional magnetic resonance imaging (fMRI), which further correlated with more binge-drinking during the weekend. They further showed a positive link between the weekend social jetlag and post-weekend neural responses to anticipated rewards. The study provided preliminary evidence for the association between sleep/circadian disruption and the activity of neural circuits underlying reward signaling in human adolescent subjects.

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Using a rodent model, the causal link between early-life sleep deprivation and reward-seeking behavior in adolescence was further interrogated by Atrooz et al.. The authors adopted a 14-day sleep deprivation protocol using a rotating bar setup during the pre-adolescent period from postnatal day (PND) 19 to PND32 in rats. After the conclusion of sleep deprivation protocol, at PND33, the authors examined the rats for anxiety-like and depression-like behaviors using the elevated plus maze test and the sucrose splash test, respectively. They also assessed alcohol consumption in rats at the adolescent stage starting at PND39 for five consecutive days using voluntary alcohol drinking test. They found that compared to the control rats, the sleep deprived (SD) animals spent significantly less time in the open arm in the elevated plus-maze test and reduced grooming in the sucrose splash test, suggesting increased anxiety- and depression-like behaviors. When the animals grew to become adolescents, interestingly, SD rats showed significantly increased consumption of alcohol together with an elevated alcohol preference over water as compared to control rats, likely due to prior sleep deprivation.

As suggested by these two intriguing studies, adequate sleep during development is believed to play a critical role in shaping important brain functions. Emerging evidence has revealed that persistent sleep disturbances during early life developmental stages (e.g., early childhood, adolescence) are likely to lead to negative consequences including substance use and abuse, and under pathological conditions may contribute to the progression of mental illnesses. Alrousan and colleagues further reviewed a large body of literature in Alrousan et al. and discussed the link between sleep and postnatal

brain development, the molecular mechanisms that might be involved, and the available animal models based on knowledge and insights gained from recent human and animal studies.

What are the structural underpinnings of sleep's developmental role? In an attempt to tackle this question, Brodin et al. compared the dendrite and spine morphology of hippocampal CA1 pyramidal neurons in adult mice after acute single sleep deprivation challenge with that in the control mice, using the tissue-clearing technique, See Ke et al., 2016. However, the authors found no significant change in the dendritic arborization or spine density/morphology in the CA1 pyramidal neurons. The authors suggested that a single episode of sleep deprivation has no major neuroanatomical changes. On the other hand, given the previous studies demonstrating that sleep does regulate the dynamics and ultrastructure of cortical and hippocampal spines in juvenile mice (Maret et al., 2011; Yang et al., 2014; de Vivo et al., 2017; Li et al., 2017; Spano et al., 2019; Zhou et al., 2020; Nagai et al., 2021), it is also likely that the impact of sleep deprivation on dendritic spines is more profound during development than in adulthood.

We hope that this Research Topic brings intriguing insights to our readers regarding the impact of sleep deprivation during developmental stages on reward seeking behavior and mental health of adolescents.

## AUTHOR CONTRIBUTIONS

W-JB wrote the manuscript with contributions from FA, SP, and AR.

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