A candidate-based screen to identify genes involved in sleep maturation

Hayley H. Kim1, Jeffrey B. Rosa2, Matthew S. Kayser2

1College of Arts and Sciences Class of 2025, 2Departments of Neuroscience and Psychiatry, Perelman School of Medicine

Funded by the College Alumni Society, Penn Career Services Summer Funding, NIH R01NS120979, and the Simons Foundation Autism Research Initiative

Abstract

Sleep is a universal behavior among animals, despite leaving them defenseless and unable to carry out essential activities – suggesting an essential function. In early life, sleep is thought to promote brain and behavior maturation. Consistent with a privileged function, sleep in early postnatal life is qualitatively distinct from adult sleep, characterized by increased sleep duration, depth, and architecture. The molecular control mechanisms underlying juvenile sleep and sleep maturation are poorly defined. The vingear fly Drosophila melanogaster is a powerful organism to study juvenile sleep due to its wealth of tools to allow gene manipulation, like humans, juvenile flies (0–1 day after eclosion) sleep longer, and more deeply, than mature adults (~1 week old).

Moreover, sleep in Drosophila is regulated by conserved neurotransmitter systems, including dopamine (DA), an arousal-promoting cue. Previous work demonstrated that sleep maturation is controlled by changes to DA tone, resulting in increased arousals during sleep. The molecular basis of this change remains entirely uncharacterized. To identify genes acting in adult dopaminergic neurons (DANs) to drive sleep maturation, we hypothesized that changes in gene transcription in DANs cause changes in DA activity to drive sleep maturation. To test this hypothesis, we identified differentially expressed genes between juvenile (0–1 day old) and mature (6 and 9 day old) DANs from publicly available scRNA-seq data of the adult fly brain. Candidate genes were systematically knocked down in DANs using short hairpin RNAs to screen for conditions that caused sleepy mature flies, suggesting a potential defect in sleep maturation. To enrich for genes acting preferentially in juvenile DANs, we followed a biphasic screen for conditions that caused sleepy mature flies, suggesting a potential defect in sleep maturation. The molecular basis of this change remains entirely uncharacterized.

Is microtubule regulation important for sleep maturation?

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