Dysfunction in circadian behavior and physiology in mouse models of Huntington’s disease

[abstract]

Many patients with Huntington’s disease (HD) exhibit disturbances in their sleep/wake cycles as part of their symptoms. These patients have difficulty sleeping at night and staying awake during the day, which has a profound impact on the quality of life of the patients and their caregivers. It is increasingly clear that a robust sleep/wake cycle is a critical component of good health. In this study, we examined diurnal and circadian rhythms of several models of HD mouse models. These mouse showed profound circadian phenotypes as measured by wheel-running activity. Also, the amplitude of the rhythms of HD mice declined progressively with age. To better understand the mechanistic underpinnings of the circadian disruption, we used electrophysiological tools to record from neurons within the central clock in the suprachiasmatic nucleus (SCN). The HD mice exhibit reduced rhythms in spontaneous electrical activity in SCN neurons. Interestingly, the expression of the clock gene was not altered in the SCN of the HD mouse. Together, this data is consistent with the hypothesis that the HD mutations interfere with the expression of robust circadian rhythms in behavior and physiology. The data raise the possibility that the electrical activity within the central clock itself may be altered in this disease.