

Blue light therapy improves circadian dysfunction in two mouse models of Huntington's disease

Huei-Bin Wang, Dawn H Loh, Daniel Whittaker, Danny Truong, Christopher S Colwell

Laboratory of Circadian and Sleep Medicine, Semel Institute for Neuroscience and Human Behavior, Department of Psychiatry and Biobehavioral Sciences, University of California - Los Angeles, Los Angeles CA 90095-1759

Patients with Huntington's disease (HD) exhibit movement disorders, psychiatric disturbance and cognitive impairments as the disease progresses. Abnormal sleep/wake cycles are common among HD patients. In addition to the reports of delayed sleep onset and greater sleepiness during the waking phase, the changed circadian pattern of melatonin suggests dysfunction in the circadian timing system. Moreover, previous studies in mouse models of HD have demonstrated that the circadian rhythm system in HD is disrupted. Importantly, circadian dysfunction manifests early in disease, even before the classic motor symptoms, in both patients and mouse models. Therefore, we hypothesize that circadian dysfunction may interact with the disease and exacerbate the HD symptoms. Moreover, early intervention may benefit patients and delay disease progression. One test of this hypothesis is to determine whether light therapy designed to strengthen this intrinsic timing system can delay the disease process in mouse models of HD. Light is a strong environmental regulator of circadian timing with blue wavelength light having the strongest impact. In addition, the blue-enriched light therapy has potential benefits over current light therapy, including shorter therapy sessions, more comfortable light intensity, and energy savings. Therefore, this study applied blue-enriched light during the first 6h of light phase during the pre-manifest stage of two HD mouse models: the BACHD (3mo) and Q175 heterozygous (6mo) mouse models. After 3 months of treatment, both genotypes showed improvements in their locomotor activity rhythm and motor performance. Finally, the profound improvements of Q175 mice triggered us to further study the underlying signaling pathways and biological processes altered by blue light. Our results showed that the expression of a number of HD relevant markers were altered in the striatum and cortex of the treated mice. Our study suggested the possibility that novel environmental intervention can delay the progression of HD in pre-clinical models.

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