Irregular Sleep-Wake Rhythm Disorder

Sabra M. Abbott, MD, PhD*, Phyllis C. Zee, MD, PhD

KEYWORDS

• Circadian rhythm • Suprachiasmatic nucleus • Sleep-wake rhythm disorder • Melatonin

KEY POINTS

- Irregular sleep-wake rhythm disorder (ISWRD) is a circadian rhythm disorder in which there is no clear sleep-wake pattern present.
- ISWRD is most commonly seen in children with neurodevelopmental delays and adults with neurodegenerative disease.
- Treatments are aimed at normalizing the day-night schedule, and increasing circadian amplitude by using a combination of melatonin, light, and sleep hygiene.

INTRODUCTION: NATURE OF THE PROBLEM

Individuals normally exhibit a near 24-hour or circadian pattern of behaviors and physiology, regulated by the central circadian pacemaker located in the suprachiasmatic nucleus (SCN). Irregular sleep-wake rhythm disorder (ISWRD) is a circadian rhythm disorder where there is no longer a clear 24-hour sleep-wake pattern. Individuals present with symptoms of either insomnia, excessive daytime sleepiness, or both, related to being awake during traditional sleep periods, and napping during the daytime.[1] The diagnosis of ISWRD depends on obtaining sleep-logs and/or actigraphy recordings from the individual for at least 1 but preferably 2 weeks. Sleep logs generally need to be completed by a caretaker given the high prevalence of neurologic impairment associated with this disorder. Actigraphy and sleep logs demonstrate at least three distinct sleep episodes within a 24-hour period; however, the total sleep for the entire day should be within normal limits for age (**Fig. 1**).[2,3] Usually sleep patterns consist of a slightly longer bout of sleep at night, with multiple naps throughout the day.

There are many factors that likely contribute to the development of ISWRD. There can be dysfunction at the level of the central pacemaker, the SCN, resulting in difficulty maintaining a 24-hour rhythm. There can also be pathology at the level of input to the SCN, either through impaired light pathways caused by retinal or optic nerve dysfunction, or through abnormal melatonin secretion. Finally, alterations in the social environment, with a lack of a clear day-night pattern, as can often be encountered in the nursing home or institutional environment can also contribute to development of this disorder. Just as the potential pathology of ISWRD is multifactorial, the populations that are affected by it are also quite diverse. Affected individuals can range from children with neurodevelopmental disorders to adults with neurodegenerative disease. An irregular sleep-wake rhythm can also be seen in some psychiatric disorders, with schizophrenia being the most frequently described. This disorder can result in significant negative consequences, particularly for caregivers who experience significant disruption to their own sleep as a result of the patient's inability to sleep through the night.

Disclosures: Dr S.M. Abbott has nothing to disclose. Dr P.C. Zee has served as a consultant for Vanda, Philips, Merck, and owns stock in Teva.
Department of Neurology, Northwestern Feinberg School of Medicine, 710 North Lake Shore Drive, Chicago, IL 60611, USA
* Corresponding author.
E-mail address: sabra.abbott@northwestern.edu

Sleep Med Clin 10 (2015) 517–522
http://dx.doi.org/10.1016/j.jsmc.2015.08.005
1556-407X/15/$ – see front matter

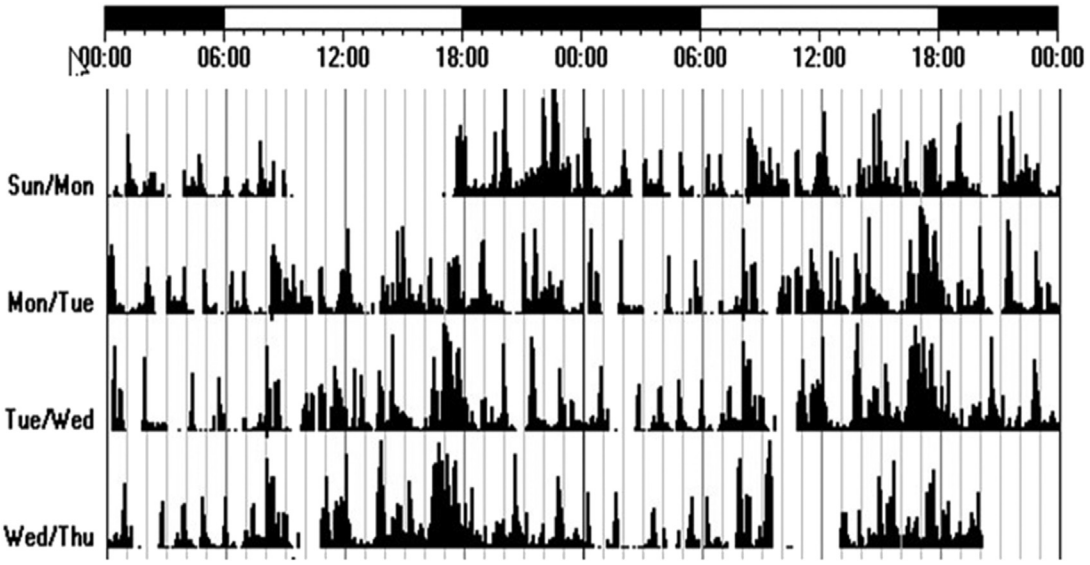

Fig. 1. Four days of actigraphy data from an individual with irregular sleep-wake rhythm disorder. Each line represents 48 hours, with the last 24 hours of each line replotted on the following line. Vertical black lines indicate activity. There is no clear rest activity pattern noted.

Many neurodevelopmental disorders in children have been associated with ISWRD. In a case series of four congenitally blind, neurodevelopmentally delayed children, most exhibited a non-24-hour or free-running pattern; however, one exhibited an irregular rest activity pattern, suggesting impairment of light input to the SCN and a primary impairment at the level of the circadian pacemaker.[4] Patients with neuronal ceroid-lipofuscinosis, a neurodegenerative disorder associated with impaired cognition and optic atrophy and retinal degeneration, frequently exhibit an irregular sleep-wake pattern. However, despite abnormal rest activity patterns, the daily rhythms of melatonin and cortisol do not seem to be significantly disrupted in these individuals, only becoming disrupted late in the course of the illness. In addition, core body temperature rhythms were only disrupted in approximately half of the children studied, suggesting the primary pathology may stem from the lack of visual input secondary to the optic atrophy and retinal degeneration.[5]

In patients with Angelman syndrome, a neurodevelopmental disorder characterized by mental retardation, seizures, gait and speech impairment, epilepsy, and craniofacial abnormalities, circadian rhythm sleep-wake disorders are common. ISWRD occurs most frequently, but delayed sleep-wake phase disorder and non-24-hour sleep-wake rhythm disorder have also been observed. These individuals have also been noted to have a decrease in nocturnal melatonin levels corresponding with their sleep-wake disturbances.[6] Smith-Magenis syndrome is a genetic disorder characterized by behavioral problems, craniofacial abnormalities, and sleep disturbances, thought to be related to abnormal melatonin secretion patterns. Although the most common sleep disturbance observed is a complete inversion of the sleep-wake schedule, these individuals also occasionally present with ISWRD.[7] Finally, children with autism spectrum disorder have also been demonstrated to have an irregular sleep-wake pattern, thought in part to be caused by an increased sensitivity to external noise resulting in greater sleep fragmentation.[8]

In a case series of elderly patients with dementia, caretaker assessments of the sleep-wake pattern demonstrated either inverted or irregular sleep-wake patterns in most individuals, with an overall decrease in the amplitude of the rest-activity rhythm. In addition, this decreased amplitude corresponded with abnormal patterns of the core body temperature rhythm.[9] Later studies have demonstrated similar findings with wrist actigraphy monitoring, demonstrating decreased overall activity, decreased circadian amplitude, and increased fragmentation of the rest-activity rhythm in patients with dementia.[10] Interestingly, the magnitude of decreased rest-activity amplitude correlates with the severity of dementia.[10] Also, increased fragmentation of the rest-activity pattern correlates with greater impairment in cognitive performance.[11]

Both aging and Alzheimer disease (AD) have also been associated with a decrease in amplitude of