PRADER-WILLI SYNDROME ASSOCIATION
Still hungry for a cure.

Sleep Problems in Prader-Willi Syndrome

By: Jan Forster, M.D. Pittsburgh Partnership, Pittsburgh, PA

Sleep problems occur frequently among individuals with PWS. The most common problem is excessive daytime sleepiness (EDS). Sometimes EDS is related to sleep apnea that disrupts the quality and efficiency of sleep. Obstructive sleep apnea is associated with increasing body mass index (BMI). Central sleep apnea occurs independent of BMI. Many of our individuals experience oxygen desaturations as a result of these apneas, but some of this hypoxemia can occur independent of apnea or hypopnea. It is common for our individuals with PWS to receive sleep studies to investigate the occurrence of apnea or oxygen desaturation.

Sleep apnea can interrupt the continuity of sleep, and these disruptions result in a decrease in both the quality and quantity of sleep. Excessive daytime sleepiness can result from this decrease in sleep efficiency. Typical individuals experience many cycles of REM (rapid eye movement) sleep and NREM (non-rapid eye movement sleep) through the night. Each sleep cycle lasts 90-120 minutes. At the onset of sleep, NREM sleep dominates the cycle; as the night progresses, REM sleep (dream sleep) dominates the cycle. The coordination of these sleep cycles is controlled in the hypothalamus. If a typical individual sleeps only 4 hours but usually requires 8 hours, they satisfy their requirement for NREM sleep, but they need to make up for the loss of REM sleep. The sleepiness that they experience the next day is associated with the intrusion of REM sleep into their wakefulness; this is taken away by a planned nap or possibly experienced as an involuntary "cat nap."

Due to hypothalamic dysfunction, individuals with PWS have intrinsic abnormalities of sleep/wake cycles. They have more sleep cycles per night and more REM periods, but the overall amount of REM sleep is decreased. Further, their sleep efficiency may be compromised by the occurrence of apneas, increasing their "sleep debt" on a daily basis. Because excessive daytime sleepiness has been correlated with the intrusion of REM sleep into wakefulness, individuals with PWS may appear to have narcolepsy-like symptoms.

Narcolepsy is a sleep disorder originally described as sleep attacks, an irresistible urge to sleep. However the majority of individuals with the condition display EDS. Narcolepsy is a disorder affecting the cycles of sleep resulting in sleep fragmentation and the intrusion of REM sleep into wakefulness. In fact, the associated symptoms of narcolepsy are related to this phenomenon: cataplexy (the sudden loss of muscle control in response to strong emotions); hypnagogic hallucinations (vivid dreams at sleep onset); hypnopompic hallucinations (vivid dreams just before awakening); and sleep paralysis (inability to move voluntary muscles during the transition between wakefulness and sleep). REM sleep is associated with a loss of voluntary motor control that prevents the acting out of dreams. Sleep paralysis and cataplexy are the manifestation of this loss of voluntary motor control intruding into wakefulness. Narcolepsy occurs with or without cataplexy; and occasionally, cataplexy occurs without narcolepsy. (For example, because antidepressants suppress REM sleep, their discontinuation has been noted to cause REM rebound and the precipitation of attacks of cataplexy.) Narcolepsy is diagnosed by clinical findings and by the results of the Multiple Sleep Latency Test (MSLT). In contrast to the nighttime sleep studies that most of our individuals with PWS receive, the MSLT is performed 4-5 times through the day in the sleep lab at 2-hour intervals, measuring the onset of sleep and REM periods during naps. In narcolepsy the time that it takes to fall asleep is very short, and the time that it takes to experience a REM period is similarly shortened. A hereditary form of narcolepsy has been described, but narcolepsy also occurs as a result of central nervous system dysfunction when the function of the hypothalamus is impaired. Some individuals with PWS have also been diagnosed with narcolepsy. Because most individuals with PWS who have EDS receive nighttime sleep studies to look for sleep apneas, the findings associated with the daytime MSLT have not been systematically explored. Further, it is possible that the narcolepsy-like symptoms in PWS are the result of sleep deprivation due to sleep apnea or disruption by other intrinsic factors.

The treatment of excessive daytime sleepiness and narcolepsy are similar. The first intervention is to improve sleep hygiene by shaping behavior to assure the appropriate amount of sleep and to supplement this with planned naps, if necessary. The second intervention is to treat the source of sleep disruption; CPAP or BIPAP are needed for obstructive sleep apnea or intermittent hypoxemia. Then, the daytime use of stimulant medication (either methylphenidate or dextroamphetamine derivatives) and/or modafinil (Provigil) is recommended. In select situations with careful monitoring, both stimulants and modafinil may be administered more than once per day if needed, but not too close to bedtime as they might interfere with sleep onset. Modafinil is approved for treatment of narcolepsy and excessive daytime sleepiness, but a copy of the sleep study may be required to authorize its use for EDS. Many individuals who have EDS for any reason have difficulty with attention span and memory. Therefore, improving sleep efficiency and using stimulant medication to treat residual symptoms will improve level of function. Of all of the narcolepsy symptoms, cataplexy is the most difficult to treat and may require consultation with a neuropsychiatric sleep specialist.

Prader-Willi Syndrome Association (USA), 8588 Potter Park Drive, Suite 500, Sarasota, Florida 34238
800– 926-4797 * 941-312-0400 * Fax: 941-312-0142 * info@pwsausa.org * www.pwsausa.org

MA-345
11/2014