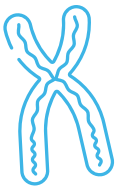
What is Prader-Willi Syndrome (PWS)?

ACADIA



Prader-Willi syndrome (PWS) is a **rare, neurobehavioral genetic disorder** that is estimated to affect 8,000 to 10,000 patients in the United States.[1-3]

This condition is caused by **abnormalities on chromosome 15** including gene deletion, uniparental disomy and imprinting mutation with symptoms varying by individual.[1] There is currently no cure for PWS.[1]

How is PWS diagnosed?

Doctors use blood and saliva based genetic tests to identify PWS. The preferred test is DNA methylation testing, which detects over 99% of PWS cases and checks for all three genetic subtypes.[1]

What are the common symptoms of PWS?

A key feature of PWS is hyperphagia, which is an unrelenting lack of satiety.[1] Studies suggest that defects in the normal function of oxytocin may contribute to the severe hyperphagia and other behavioral symptoms characteristic of PWS.[4-5]

Other defining features of the syndrome may include altered metabolism, developmental delays, behavioral challenges and moderate cognitive deficits.[1] Patients may also experience high pain tolerance, digestive problems, breathing problems during sleep disturbances, gastrointestinal issues, respiratory and temperature regulation abnormalities.[1]

WHAT IS HYPERPHAGIA?

Hyperphagia in PWS is associated with:[8]

- **lack of a normal satiety**
- **food preoccupations**
- **an extreme drive to consume food**
- **food-related behavior problems**

If left unsupervised, patients with hyperphagia are known to eat to the point of gastric rupture.[6,7] Those living with PWS also have a greater propensity to choke while eating.[7]

What is the unmet need in PWS?

PWS presents with a variety of symptoms and medical issues that create challenges for the people living with this condition and their families.[6] As those diagnosed with PWS get older, hyperphagia, maladaptive behaviors, and obesity significantly affect their day-to-day living, impacting their independence and daily functioning.[6]

In one study, out of all common symptoms of PWS, hyperphagia was determined as a major contributor to caregiver burden.[7] Due to the risks of overeating to the point of gastric rupture and swallowing problems, hyperphagic patients require constant supervision and a consistently controlled food environment.[6,7] According to one survey, hyperphagia and difficult behavior around food were identified as the most concerning symptoms for caregivers.[6]

1. Prader-Willi Syndrome Association. What Is Prader-Willi Syndrome? Retrieved from https:// www.pwsausa.org/what-is-prader-willi-syndrome/. Accessed January 17, 2024. **2.** McCandless SE, Suh M, Yin D, et al. SUN-604 U.S. Prevalence & Mortality of Prader-Willi Syndrome: A Population-Based Study of Medical Claims. *J Ednocr Soc.* 2020;4 (Suppl 1): SUN-604. **3.** Acadia Pharmaceuticals Inc. Data on File. *PWS Prevalence Rate.* 2023. **4.** Swaab DF, Purba JS, and Hofman MA. Alterations in the hypothalamic paraventricular nucleus and its oxytocin neurons (putative satiety cells) in Prader-Willi syndrome: a study of five cases. *J Clin Endocrinol Metab.* 1995;80(2):573-579. **5.** Bittel, DC, Nataliya K, Sell SM, et al. Whole Genome Micaroarray Analysis of Gene Expression in Prader-Willi Syndrome. *Am J Med Genet A.* 2007; 143A((5):430-442. **6.** FPWR. Summary of the Impact of PWS on Individuals and Their Families and Views on Treatments: Results of an International Online Survey. 2014. Retrieved from: //fpwr.org/hubfs/PDFs/Patient%20Voices_graphic%20novel_Nov_topostFinal.pdf? hsCtaTracking=2c814cf5-d916-413c-9710-234407b8974e%7C99e41f73-683b-4635-940d-952bf8a93499. Accessed January 17, 2024. **7.** Kayadjanian N, Vrana-Diaz C, Bohonowych J, et al. Characteristics and relationship between hyperphagia, anxiety, behavioral challenges and caregiver burden in Prader-Willi syndrome. *PloS ONE.* 2021;16(3):e0248739. **8.** FPWR. Hyperphagia in Prader-Willi Syndrome. Retrieved from https://www.fpwr.org/hyperphagia-in-prader-willi-syndrome#managing_hyperphagia. Accessed January 17, 2024.