

What is a rare melanocortin-4 receptor pathway disease?

Rare melanocortin-4 receptor (MC4R) pathway diseases can be caused by genetic variants within the MC4R pathway (part of the central melanocortin pathway).¹

This can impair signalling in the pathway that controls hunger, leading to hyperphagia (pathological, insatiable hunger) and increased body weight.¹

Characteristics and behaviours of hyperphagia²



Heightened and prolonged hunger



Severe preoccupation with food
(hyperphagic drive)



Longer time to reach satiety



Food-seeking behaviours
(sneaking or stealing food)



Shorter duration of satiety



Distress and functional impairment if denied food

Should your patient be evaluated for a rare MC4R pathway disease?

Look for the following signs³⁻⁴



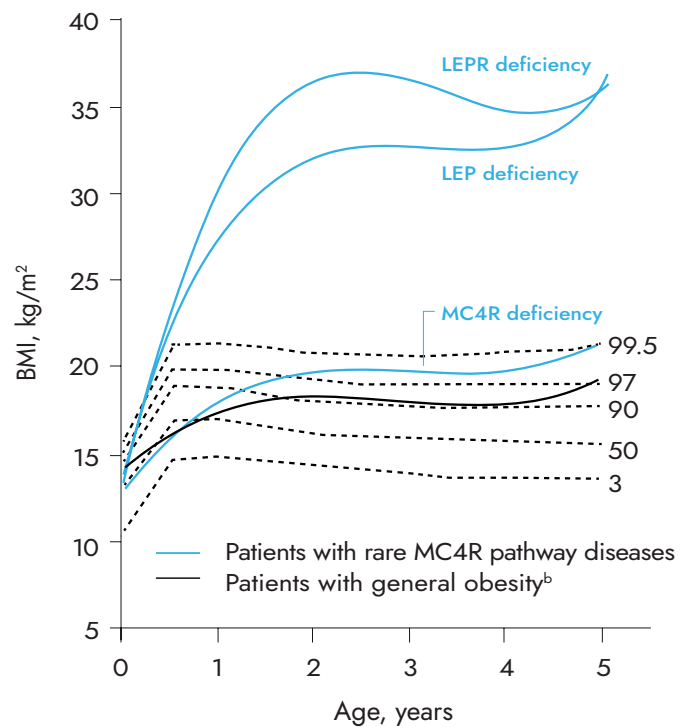
Hyperphagia



Early-onset, severe obesity^a

a) Defined as having a BMI $\geq 120\%$ of the 95th percentile and onset before the age of 5.

Growth curves in patients with early-onset, severe obesity⁵



b) Patients with general obesity have a BMI >30 kg/m² by age 14 to 16 years and do not have a variant in *LEP*, *LEPR*, or *MC4R*.

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References: 1. Loos RJF and Yeo GSH. *Nat Rev Genet*. 2022;23:120–133. 2. Heymsfield SB, et al. *Obesity (Silver Spring)*. 2014;22(suppl 1):S1–S17. 3. Huvenne H, et al. *Obes Facts*. 2016;9(3):158–173. 4. Hampl SE, et al. *Pediatrics*. 2023;151(2):e2022060640. 5. Kohlsdorf K, et al. *Int J Obes (Lond)*. 2018;42(9):1602–1609.

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